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Neuropsychological Patterns of Functioning of Positive, Negative and Mixed Symptom Schizophrenics

©

by

Stephanie Ann Mitchell

A Thesis

Submitted to the Faculty of Graduate Studies

And Research

In Partial Fulfilment of the Requirements for

The Degree of

Doctor of Philosophy

in School Psychology

Department of Educational Psychology

Edmonton, Alberta

Fall, 1988

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Abstract

To evaluate cognitive functioning and clinical symptom patterns, the performance of 53 schizophrenic patients on intellectual, neuropsychological and symptom rating test measures was analysed. Subjects were subgrouped into homogeneous clusters through a variety of means for the purpose of assessing the nature of cognitive deficit profiles inherent within the subgroups. The concept of a Positive and Negative symptom syndrome formed the basis for some of the subgroupings as some researchers, most notably Timothy Crow and Nancy Andreasen, have suggested that Positive and Negative schizophrenia may actually represent different disease entities.

A preponderance of male subjects form the study population (74%) as is often found among schizophrenics. Low Average intellectual functioning as well as poor cognitive functioning generally was evident for the schizophrenic group as a whole. Among the subgrouping of Positive and Negative symptom schizophrenics it was noted that comparatively few schizophrenics met the rigorous diagnostic criteria for either Positive (21%) or Negative Symptom schizophrenia (21%), with most of the study population being characterized by mixtures of both positive and negative symptoms. Within the small group identified

as a Positive symptom group, Low Average to Average intellectual functioning was evident with very mild dysfunction of neuropsychological performance. In contrast, the Negative symptom group was characterized by bilateral frontal-temporal impairment with emphasis in the dominant hemisphere language functions. Within the mixed symptom subgroupings, a group emerged that was characterized by severe, global and diffuse cognitive impairment, still with discernible left-hemispheric emphasis as well as being distinctly more symptomatic with a preponderance of both positive and negative symptoms of virtually equal magnitude. These results are discussed with reference to theories of the underlying pathogenesis as they relate to Kraepelin, Crow and Andreasen's theories of schizophrenia. In particular, research emphasis on the Positive/Negative dimension of schizophrenia, although appearing to be a valid construct, is discussed as being potentially misleadingly representative of schizophrenia as the vast majority of schizophrenics in this study had a mixture of symptoms.

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CHAPTER 1

STATEMENT OF PURPOSE

A. Introduction

It is generally agreed by researchers and practitioners that schizophrenia is not a unitary disease; rather, it is considered a heterogeneous syndrome composed of a number of subtypes which vary in etiology, pathogenesis, clinical picture and course, response to treatment, and outcome (Kaplan and Sadock, 1985; Kety, 1980; Baldesarrini, 1977). Despite the wide recognition of its heterogeneity, critical parameters that unify or discriminate subtypes are not yet well defined.

Initial efforts of Emil Kraepelin in the late 1800's provided an amalgamation of a cluster of symptoms forming the genesis of the disorder we now call schizophrenia. Since then, there has been a consistently dichotomous clustering of symptoms found in clinical descriptions of the schizophrenic syndrome. Consistently, a clustering of an actively florid set of symptoms contrasts with a more passive, defect state, and this duality of qualitatively distinct clusters of symptoms has remained

stable across time, albeit under different names. The more active, florid symptoms are often called "positive" symptoms, while the passive, defect state is called "negative" symptoms. The stable presence across time of the concept of negative/positive symptom patterns in clinical descriptions is qualitative evidence of the validity of the construct. However, until recently, reliable measurement of positive and negative symptoms has been limited (Kulhara, Kota and Joseph, 1986).

There is a wide variety of data consistent with the hypothesis that positive and negative symptoms of schizophrenia reflect different disease entities (Andreasen, 1982; Crow, 1980; Dworkin, Lenzenweger, 1984). Many researchers have provided evidence that schizophrenics have a higher incidence of structural brain damage than control subjects as measured through such means as CT scans (Stevens, 1982; Andreasen, Olsen, Dennert et. al., 1982; Andreasen and Olsen, 1982). There also appear to be trends emerging suggesting those brain damaged patients tend to have a higher incidence of negative symptoms (Opler, Kay, Rosado, Lindenmayer, 1984).

Presumably, there are a number of hidden subgroups within heterogeneous groupings of schizophrenics.

The etiology and pathology of these subgroups likewise undoubtedly is heterogeneous. The search for common characteristics amidst heterogeneous groups potentially contaminates information that could lead to identifying etiological factors underlying the disorders. Identifying etiologies of schizophrenia realistically would need to take into account the recognized heterogeneity of syndromes and compare different groups of schizophrenics divided on the basis of some meaningful criteria. Thus, the dichotomy of positive and negative symptom schizophrenics may serve as such a meaningful division.

This research project was undertaken to assess schizophrenics primarily from the perspective of two major factors (namely, the clinical symptom pattern of positive, negative or mixed syndromes, as well as patterns of neuropsychological functions), and to comprehensively assess the quantitative and qualitative interplay of these factors. Neuropsychological tests are often used simply as a means of ruling out organicity in clinical populations. Golden (1983) suggests these tests may be effectively used to evaluate the relationship of organic and psychiatric factors, rather than simply to rule out organicity. The primary goal of this study is to evaluate the interaction between the clinical manifestation of symptoms and corresponding neuropsychological deficit patterns.

The practical goal of this research is to contribute to a better understanding of brain-related functions of schizophrenics. Such information is of significance for the development of knowledge of the etiologies of different syndrome patterns among schizophrenics, and establishment of more effective treatment interventions.

B. Statement of Purpose

Specific objectives of this research project are: (1) to determine if there are significant differences between positive, negative and mixed symptom schizophrenics in the degree to which they will manifest neuropsychological deficits as measured by the Halstead-Reitan Neuropsychological Test Battery; (2) to assess the possibility that a specific patterning of neuropsychological deficits will emerge within the parameters of the positive, negative and mixed subdivisions. Through so doing, it is hoped a better understanding of the nature of brain-behavior relationships and brain deficits among schizophrenics will be gained which may provide clues to the etiologies of these apparent subtypes.

CHAPTER II

THEORIES AND DIAGNOSTIC SYSTEMS IN SCHIZOPHRENIA

A. Introduction

Theories of schizophrenia, the distinction between disease entity versus syndrome, and the notion of brain-behavior relationships are all fundamental constructs to this research project. This theoretical chapter contains a brief outline of the more widely accepted theories of schizophrenia, discussed from a historical perspective. Beginning with the initial description of schizophrenia as a hypothetical disease entity, various significant theories are discussed including genetic, developmental/environmental, biochemical and, more generally, pathological brain functions typically associated with schizophrenia. Following the description of the theories regarding etiology and pathogenesis, diagnostic systems of the syndrome are reviewed, with a focus on distinguishing a known disease entity from a syndrome and the limitations this inevitably creates for research on this population. Finally, a theory of brain-behavior relationships and a conceptual model of behavioral correlates of cerebral functioning is presented.

B. Theories of Schizophrenia

(a) Emil Kraepelin

Schizophrenia was first described as a disease entity in 1985 by Emil Kraepelin who grouped together a number of features, each previously considered to be separate disease entities. The term he used to describe this collection of symptoms was dementia precox. The primary symptoms incorporated included a wide range of abnormalities in perception, attention, memory, thought, language, orientation, volition, affect, and bodily movements, as well as many types of delusions and hallucinations, the presence of which predicted inevitable deterioration. Kraepelin's conception of dementia precox was that clinical phenomena were the result of one morbid process at work. He believed dementia precox to be a single disease entity that probably had a similar cerebral pathology. The nature of the pathology appeared to result in the unremitting deterioration similar to that of a dementia.

(b) Eugene Bleuler

The bleak prognosis predicted by Kraepelin did not always prove to be the case, however. In 1911 Eugene

Bleuler observed that the clinical phenomena detailed by Kraepelin were not always associated with an incurably progressive deterioration, and he reconceptualized the problem as both a disease entity as well as a psychopathological reaction or syndrome, which he called schizophrenia. For some patients the course could be expected to be a progressive deterioration, while for others recovery would occur. Bleuler's reformulation of Kraepelin's concept stressed productive features of the clinical picture, namely, hallucinations, delusions, and disturbances in associations, while de-emphasizing the downward course. He made a distinction between fundamental and accessory symptoms of schizophrenia and referred to the "core" symptoms as being abnormalities in association, affect, ambivalence, relationship to reality, attention, volition, and sense of identity or ego function. Delusions and hallucinations he considered to be examples of "accessory" symptoms. In effect, Bleuler incorporated milder forms of the disorder, having observed that some individuals did improve.

(c) Genetic Theory

Epidemiology, as well as familial studies, especially of the twin and adoption type established a

considerable body of evidence to suggest a genetic factor is at play for some individuals suffering from schizophrenia. The following rates of incidence of schizophrenia are reported in Kaplan and Sadock (1985):

- .3-2.8% - general population and stepsiblings
- .2-12% - probands of schizophrenic parents
- 3-14% - full siblings
- 8-18% - 1 schizophrenic parent
- 15-55% - 2 schizophrenic parents

Pooled results indicate a 9% risk in siblings, 12% with 1 schizophrenic parent, 50% concordance rate for monozygotic twins and 15% for dizygotic twins. Adopted-away children of schizophrenic parents develop schizophrenia at higher rates than the general population.

It is readily observable that the degree of genetic closeness and severity increase the risk of illness, which implies an inherited component.

(d) Developmental/Environmental Theories

The schizophrenic state, characterized by an inability to cope effectively with environmental stress and personal conflicts, typically results in increased levels of anxiety. Consequently, dysfunctional avoidant and

irrelevant thoughts are acquired, presumably to reduce anxiety. Developmental hypotheses propose that this vulnerability is attributable to a genetic predisposition towards excessively strong physiological reactions to mild stress. Essentially, deficient ego functioning, whether attributable to psychophysiological or developmental factors reduces the schizophrenics' capacity to handle their environment, according to developmental/environmental theorists.

(e) Dopamine Hypothesis

The administration of antipsychotic drugs to schizophrenic patients has provided much of the evidence from which the dopamine hypothesis of schizophrenia emerged. In this theory, behavioral symptoms are considered to be reflective of central dopaminergic overactivity; that is, symptoms of the disorder relate to an increased amount of dopamine at the neural synapses. The evidence in favor of this hypothesis is strong. Drugs acting to decrease dopaminergic activity by blocking the receptor sites can reduce schizophrenic symptoms, (Carlsson and Lindquist, 1963; Matthysse, 1973; Yaryura-Tobas, Diamond and Merlin, 1970). It has been well established that for some schizophrenics neuroleptic medications reduce

symptoms, thus providing convincing evidence of a defective dopaminergic system. However, the nature of this deficit and its role in schizophrenia is not yet clearly understood. The dopamine deficit may simply be an expression of some other pathophysiological defect, the nature of which is not yet understood (Kaplan and Sadock, 1985).

(f) Neurological Abnormalities in Children

Neurological abnormalities hypothesized to be due to genetic, intrauterine, or perinatal complications (e.g., viral infections, lags in maturation of the brain, etc.) can predict the emergence of schizophrenia in some cases and may provide clues regarding etiologies. Children predisposed to schizophrenia are characterized by a variety of early symptoms including disturbed regulation of physiological patterns (vasomotor instability, disturbed sleep pattern, poor temperature control, poor muscle tone and alertness, uneven pattern of growth, retardation or precocity in motor, perceptual and language skills and in the social sphere); peculiarities of gait, motor awkwardness, postural disturbance, change in muscle tone and sudden unexplained movements; lower I.Q.; auditory and visual information cannot be integrated; poor hand-to-hand

integration; poor visual-motor integration. Of course, these deficits can also occur in children who do not develop schizophrenia, and so their significance is not yet established. Perhaps differential diagnostic patterns may emerge as the sophistication of our neuropsychological instruments increases.

C. Diagnostic Systems of Schizophrenia

(a) Bleuler, Langfeldt, Schneider

The diagnostic systems of Bleuler, Landfeldt, and Schneider each incorporate a duality of symptom clustering. As previously discussed, Bleuler's diagnostic system for schizophrenia includes the notion of primary symptoms, which are flat or inappropriate affect, loose associations, ambivalence and autism known as the 'four A's'), and secondary symptoms (e.g., hallucinations, delusions). Gabriel Langfeldt's diagnostic criteria include a concept of "true" schizophrenia, also referred to as "process", "nuclear" or "nonremitting" schizophrenia as distinct from schizophreniform psychosis. The true schizophrenia is characterized by depersonalization, autism, emotional blunting, insidious onset, and feelings of derealization and unreality. Kurt Schneider made a division on the basis of "first-ranked" and "second-ranked" symptoms. The

"first-ranked" symptoms include thought broadcasting, auditory hallucinations, somatic hallucinations, thought control, delusions, and the experience of having one's actions controlled or influenced from the outside. "Second-ranked" symptoms include other forms of hallucinations, perplexity, depressive and euphoric affective disorders, and emotional blunting. The Schneiderian "first-ranked" symptoms were considered to have pragmatic value in making a diagnosis. Although Schneider states clearly that a diagnosis can also be made exclusively on the basis of "second-ranked" symptoms, many clinicians tend to rely heavily on the presence of "first-ranked" symptoms and to a large extent ignore the "second-ranked" symptoms when making a diagnosis (Kaplan and Sadock, 1985).

The duality present in the evolution of these diagnostic systems reflects the stability of the two qualitatively distinct symptom clusters which has persisted over time.

(b) D.S.M.-III Classification

The present classification system in use in many clinical settings is the D.S.M.-III (1980). The diagnostic

criteria for schizophrenia in this manual are:

Diagnostic criteria for a Schizophrenic Disorder

A. At least one of the following during a phase of the illness.

(1) bizarre delusions (content is patently absurd and has no possible basis in fact), such as delusions of being controlled, thought broadcasting, thought insertion, or thought withdrawal

(2) somatic grandiose, religious, nihilistic, or other delusions with persecutory or jealous content if accompanied by hallucinations of any type

(3) delusions with persecutory or jealous content if accompanied by hallucinations of any type

(4) auditory hallucinations in which either a voice keeps up a running commentary on the individual's behavior or thoughts, or two or more voices converse with each other

(5) auditory hallucinations on several occasions with content of more than one or two words, having no apparent relation to depression or elation

(6) incoherence, marked loosening of associations, markedly illogical thinking, or marked poverty of speech associated with at least one of the following:

(a) blunted, flat, or inappropriate affect
(b) delusions or hallucinations
(c) catatonic or other grossly disorganized behavior

B. Deterioration from a previous level of functioning in such areas as work, social relations, and self-care.

C. Duration: Continuous signs of the illness for at least six months at some time during the person's life, with some signs of the illness at present. The six-month period must include an active phase during which there were symptoms

from A, with or without a prodromal or residual phase.

Prodromal phase: A clear deterioration in functioning before the active phase of the illness not due to a disturbance in mood or to a Substance Use Disorder and involving at least two of the symptoms noted below.

Residual phase: Persistence, following the active phase of the illness, of at least two of the symptoms noted below, not due to a disturbance in mood or to a Substance Use Disorder.

Prodromal or Residual Symptoms

(1) social isolation or withdrawal

(2) marked impairment in role functioning as wage-earner, student, or homemaker
(3) markedly peculiar behavior (e.g., collecting garbage, talking to self in public, or hoarding food)
(4) marked impairment in personal hygiene & grooming
(5) blunted, flat, or inappropriate affect
(6) digressive, vague, overelaborate, circumstantial
(7) odd or bizarre ideation, or magical thinking (e.g., superstitiousness, clairvoyance, telepathy, "sixth sense" "others can feel my feelings" overvalued ideas, ideas of reference
(8) unusual perceptual experiences, e.g., recurrent illusions, sensing the presence of a force or person not actually present

Examples: Six months of prodromal symptoms with one week of symptoms from A; no prodromal symptoms with six months of symptoms from A; no prodromal symptoms with two weeks of symptoms from A and six months of residual symptoms; six months of symptoms from A, apparently followed by several years of complete remission with one week of symptoms in A in current episode.

D. The full depressive or manic syndrome (criteria A and B or major depressive or manic episode), if present, developed after any psychotic symptoms, or was brief in duration relative to the duration of the psychotic symptoms in A

E. Onset of prodromal or active phase of illness before age 45.

F. Not due to any Organic Mental Disorder or Mental Retardation.

(c) Summary of Evolution of Theory and Diagnostic Classifications

Bleuler's view prevailed for many years. However, during the past twenty years the emphasis has shifted from Bleuler's "core" symptoms (once considered the primary determinants for a diagnosis of schizophrenia) to hallucinations and delusions, which Bleuler had originally defined as the accessory symptoms. This has likely occurred because clinicians and investigators became increasingly concerned about improving reliability of diagnosis. Emphasis on these accessory symptoms provided a means through which this could be accomplished, as the core symptoms were less easily operationalized and measured (Andreasen, 1982). In this vein, in 1957 Kurt Schneider became a forerunner in the increasingly more prevalent view that the Schneiderian "first-ranked" symptoms be seen as an infalible guide to correct diagnosis. The current Diagnostic and Statistical Manual (D.S.M.-III, 1980) reflects this emphasis on the first-ranked symptoms and largely excludes specification of the negative symptoms.

Recently, it has become apparent that some investigators feel this reliability has been accomplished at the expense of validity, as there has been a resurgence of the dichotomous approach initially proposed by Bleuler (Dworkin and Lenzenweger, 1984; Crow, 1980(a); Andreasen, 1982). In this renewed approach, the florid manifestations (e.g., thought disorder, hallucinations, delusions, and bizarre behavior) are referred to as positive symptoms, and symptoms that seemingly underlie the social and cognitive decline (e.g., impoverished speech and thinking, affective flattening, avolition, anhedonia, progressive deterioration) are referred to as negative symptoms (Opler, Kay, Rosado, and Lindenmayer, 1984).

Within this revitalized framework, Crow (1980(b)) has hypothesized a dual etiology for schizophrenia: a disturbance in dopaminergic transmission as being characteristic of the positive syndrome schizophrenic, and cellular loss reflecting structural brain damage in the negative symptom schizophrenic. His hypothesis, although thus far untested, is based on the clinical finding that positive, but not negative symptom patients respond to neuroleptic treatment (Johnstone, Crow, Frith, 1978), and chronic negative symptom schizophrenics have been found to have increased ventricular size with

intellectual deficit (Johnstone, Crow, Frith, 1978). Similarly, Andreasen, et. al. (1982) postulate that positive symptoms reflect a "release from higher cortical inhibitors", while the negative symptom syndrome is attributable to the structural changes suggested by ventricular enlargement and cerebral atrophy. In essence, negative symptoms are considered to involve a loss of function due to damage to some area of the brain; consequently, poor prognosis is more typically associated with these negative symptoms (Andreasen, 1982). In contrast, positive symptoms are considered to reflect the loss of inhibitory functions which may be altered through the use of neuroleptics, thus providing a greater likelihood of remission of these symptoms with treatment, as the symptoms are alterable through biochemical intervention.

There is a wide variety of data consistent with the hypothesis that positive and negative symptom schizophrenics reflect different disease entities with different brain abnormalities and brain-behavior functions. Poorer premorbid adjustment (Prentky, Watt, Fryer, 1979; Andreasen and Olsen, 1982), cognitive and intellectual impairment (Owens and Johnstone, 1980; Johnstone, Crow, Frith, et. al., 1978; Frith, 1977; Andreasen and Olsen,

1982), neurological signs (Owens and Johnstone, 1980), neuropathologic abnormalities and ventricular enlargement (Andreasen and Olsen, 1982; Andreasen, Olsen, Dennert, et. al., 1982; Stevens, 1982) are all associated with negative symptoms in schizophrenia. In contrast, positive symptoms are associated with a better premorbid adjustment, better response to treatment, and a better prognosis (Andreasen, 1982; Allen and Allen, 1985). However, the positive symptom schizophrenia is characterized by a primary loss of control of information processing such that the ability to organize information meaningfully and purposefully is lost (Frith, 1979; Crow, 1980; Andreasen, 1982). Appendix A contains a comprehensive and detailed description of both positive and negative symptoms developed by Andreasen (1984).

(d) Limitations of Diagnostic Systems

Schizophrenia is diagnosed on the basis of the defined signs and symptoms described. This makes it a syndrome as opposed to a known disease entity due to the fact we do not know the etiology and pathology of the disorder; to-date only theories exist. Consequently, the accuracy of diagnosis is often vulnerable to subjective interpretation and clinical judgment, despite attempts to

improve reliability through improving diagnostic classifications. In 1983, a survey of 1,227 psychiatrists in the United States revealed a lack of consistency among psychiatrists in their diagnosis of schizophrenics. The authors of the survey noted that a substantial number of psychiatrists used highly subjective or impressionistic findings in their diagnosis (Lipkowitz and Idupuganti, 1983). This fact will inevitably impose limitations on research conducted with schizophrenic populations, and thus derivation of the study group rests on somewhat nebulous, equivocal criteria. Despite diagnostic difficulties, clinical validity of the syndromes persist.

D. Theory of Brain-Behavior Relationships

(a) Evolution of Model of Brain-Behavior Relationships

The theoretical foundation upon which this research is based is one established by Ralph Reitan and W. C. Halstead regarding the theory of brain-behavior relationships. Based upon the premise that behavior functions are subserved by specific parts of the brain, measurement of observable functions allows us to make inferences about many brain-related abilities and the status of the brain.

Beginning in the 1940's, with the cooperation of neurologists, neurological surgeons and neuropathologists, Halstead and Reitan obtained careful descriptions of the brain lesions of numerous patients referred to them for evaluation. Working with these patients with known lesions, over the course of many, many years, a battery of brain-sensitive tests with established brain-behavior correlates has been developed that is considered to be of significance in identifying cerebral dysfunction. This battery is known as the Halstead-Reitan Neuropsychological Test Battery (HRNTB).

(b) Development of the HRNTB

A conceptual model of behavioral correlates of brain functions provides the theoretical foundation and rationale upon which the HRNTB was developed. Essentially, the HRNTB measures behavioral functions. From these behavioral functions inferences can be made about the status of the brain on the basis of the patient's ability to perform. The conceptual model of cerebral processing involves six heirarchically ordered levels of processing: (1) input measures (e.g., sensory perceptual functions); (2) attention, concentration and memory; (3) tests of verbal abilities; (4) measures of spatial, sequential and

manipulatory abilities; (5) tests of abstraction, reasoning, logical analysis and concept formation; and (6) output measures (e.g., motor functions). This model represents successive levels of central processing which take place in the brain and provides a useful way of conceptualizing brain-behavior relationships (Reitan and Wolfson, 1985).

The HRNTB is the most widely used battery of neuropsychological tests and is the most researched. The efficacy of the battery is well established (Golden, 1977; Halstead, 1947; Reitan and Boll, 1971; Boll, Heaton, and Reitan, 1974; Russell, Neuringer and Goldstein, 1970).

CHAPTER III

REVIEW OF RELEVANT LITERATURE

A. Introduction

Brain-behavior relationships among schizophrenics are to be explored as the fundamental purpose of this research project. As part of this intent, this chapter contains a review of relevant literature addressing, as its primary focus, the brain functioning of schizophrenics. First, a review of literature regarding the establishment of the validity and efficacy of neuropsychological testing with a schizophrenic population is presented, as this has emerged as a controversial issue historically. Secondly, since cerebral functioning of schizophrenia has been explored from a diversity of measures, a review of structural brain abnormalities, anomalies in cerebral lateralization and brain metabolism as well as cognitive deficits associated with schizophrenia is presented, with a view to linking specific findings to etiological theories.

B. Neuropsychological Impairment in Schizophrenia

(a) Introduction

Efforts to determine whether or not neuropsychological deficits reflecting brain impairment exist in schizophrenics, and the specific nature of such deficits have been fraught with many problems. Since the development of test batteries that are sensitive to brain damage, controversy has emerged and evolved regarding the use of such batteries with schizophrenic patients.

Initially, researchers questioned the efficacy of the test measures in being able to truly discriminate brain damage from other pathologies (Levine and Feirstein, 1972; Golden, C. J., 1978; Watson, Thomas, Andersen and Felling, 1968). These questions arose out of a body of literature utilizing neuropsychological test batteries with known brain damaged subjects in comparison to schizophrenic patients. Schizophrenia was considered to be a "functional" disorder and therefore it was believed schizophrenics should be distinguishable from brain damaged patients on neuropsychological batteries by virtue of their comparatively unimpaired performances on these tests. No battery or test, however, has consistently shown good results in this regard (Golden, 1978).

The following is a review of literature pertaining to the development of our present understanding

of the cerebral functioning of schizophrenics from neuropsychological test results. Briefly, research related to the efficacy and validity of using neuropsychological testing will be presented first, as it is from these initial efforts that the first clues emerged concerning the similarity of brain damaged and schizophrenic performances on neuropsychological test batteries. Secondly, factors which seemingly contribute to the degree of dysfunction found on neuropsychological tests will be reviewed, inasmuch as they have emerged in the literature as part of the controversy regarding the efficacy of neuropsychological test batteries on a schizophrenia population. Finally, research revealing the existence of brain abnormalities among schizophrenics will be reviewed from a variety of sources such as abnormalities in brain structure, cerebral lateralization, cerebral blood flow and neuropsychological functional abilities.

(b) Validity of Neuropsychological Tests in Schizophrenia

Until relatively recently, schizophrenia has been considered a "functional" disorder that should be distinguishable from known organic pathologies. The presumption that schizophrenia is not organic has lead to a search for a means of differentiating organics from

schizophrenics. Many research efforts using neuropsychological tests have been applied based on this premise with the express intent of finding the most efficacious means of distinguishing organics from schizophrenics (Brown, Casey, Fisch and Neuringer, 1958; L'Abate, Boelling, Hutton and Matthews, 1962; Orgel and McDonald, 1967; Goldberg and Smith, 1958; Johnson, Bauer and Brown, 1959; Watson and Uecker, 1966; Watson, 1967; Watson, Felling and MacEacher, 1967; Watson, Thomas, Anderson and Felling, 1968; Levine and Feirstein, 1972). The various tests used in this research have not been found to be particularly successful in making such a differentiation. This fact initially brought a dirth of criticism to the whole area and brought into question the validity of neuropsychological testing. The conclusion drawn was that if it was not possible to distinguish between schizophrenics and patients with known brain damage or disease, then the tests must be invalid.

A notable study conducted by Watson, Thomas, Andersen and Felling (1968) was an attempt to differentiate organics from schizophrenics using the HRNTB with the presumption that schizophrenia is not organic. They administered the HRNTB to 25 schizophrenics and 25 patients with cerebral lesions with the intent of determining

whether or not the HRNTB could discriminate between the two diagnostic groups. In general, the researchers concluded that the battery was not useful in differentiating schizophrenics from organics. While test performances quite accurately classified organics, a large percentage of the schizophrenic group was also classified as brain damaged. Thus, there was no significant difference between the performance of the two groups.

In contrast to Watson, et. al. (1968), Levine and Feirstein (1972) conducted a similar study with a different outcome. Their purpose was to compare the performance of three groups (oganics, schizophrenics and nonpsychiatric, non-brain damaged medical patients) on the HRNTB. Essentially, their results indicated the battery could discriminate between the groups. The brain damaged group scored in the "organic" range on an average of 5.1 of the 7 tests yielding a Halstead Impairment Index of .7; the schizophrenia group scored in the "organic" range on 3.4 of the tests yielding an Index of .5; the non-brain damaged, nonpsychiatric, medical patients scored within the "organic" range on an average of 2.7 of the tests yielding an Index of.4. While ability to discriminate between groups was the focus of Levine and Feirstein's argument, it is interesting to note that the Impairment Index for both

the brain damaged and schizophrenic groups falls within the brain damaged range, although the brain damaged group is clearly more severe. The only normally scoring group was the medical, nonpsychiatric, non-brain damaged group.

Watson, et. al. (1968) and Levine and Feirstein (1972) seem to represent opposite sides of the controversy about the validity of neuropsychological testing and the efficacy of using these measures to distinguish functional from organic and schizophrenic groups. Heaton, et. al. (1972) provided evidence of impaired cerebral functioning in schizophrenics when comparing their performance with brain damaged subjects, but found that the schizophrenics generally performed better than chronic and acute brain-lesioned patients.

The initial controversy that emerged out of this research was directed toward the efficacy of neuropsychological testing which, in the case of schizophrenics did not seem to provide convincing evidence that it could accurately discriminate functional from organic disorders. Gradually, the idea began to emerge that perhaps the tests per se were not at fault; they may well be accurately classifying schizophrenics as brain damaged, and this has lead to a host of further research

directed towards understanding the nature of dysfunctional cerebral behaviors in schizophrenics.

Another very important realization has emanated from this research. The recognition that certain methodological and subject selection factors predictably relate to the degree of impairment that is present on neuropsychological measures is beginning to reveal valuable information about the process of schizophrenia. The chronicity of the schizophrenic subjects, nature of the organic subjects (e.g., diffuse or focal damage, acute or chronic, progressive or static), the extensiveness of the test battery, method of data analysis and effects of medication are all factors which have been teased out as having a distinct bearing on results that are obtained. Following is a discussion of these factors.

(c) Factors Relating to Impairment

Chronicity. Levine and Feirstein's (1972) criticism of the Watson, et. al. (1968) research is based on two observations: (1) Watson, et. al. apparently made no overt attempts to screen their subjects for their ability to cooperate with testing procedures, and so patients were included without sufficient regard for intactness of

ability to understand the instructions: (2) A second criticism lodged was that subjects were not matched for chronicity or length of hospitalization (e.g., organic group averaged 33 months hospitalization; schizophrenic group averaged 73 months hospitalization - more than twice as long). These factors may well explain the different results found between the two studies. Levine and Feirstein, on the other hand, matched the chronicity of their subjects (e.g., organic group averaged 22 months hospitalization; schizophrenic group averaged 27 months hospitalization), and found their schizophrenic subjects less likely to perform like the brain damaged group.

In fact, this criticism has been a catalyst in developing the recognition that in general, chronicity is positively related to decrements in adaptive functioning (Purisch, Golden and Hammeke, 1978). Studies in which nonsignificant results allude to the inability of psychometric tests to discriminate between organic and schizophrenic populations have typically used long-term (e.g., over ten years) chronic schizophrenics (Watson, 1968, 1972; Watson, Thomas, Andersen and Felling, 1968; Watson, Thomas, Felling and Anderson, 1969; Watson and Uecker, 1966; Heaton, et. al., 1979). In effect, chronic schizophrenic patients look very much like brain damaged

patients in their performance on neuropsychological tests. In contrast, shorter-term (e.g., approximately one year duration) schizophrenic subjects were used in studies where reasonably accurate classification of brain damaged as distinct from schizophrenic patients was reported (Golden, 1977; Levine and Feirstein, 1972). Leaving aside the question of discriminative power of neuropsychological tests, viewing the results of the schizophrenic patients by themselves across chronicity levels certainly suggests functional deterioration as the disease progresses and would be consistent with what might be expected on the basis of Kraepelin's dementia precox.

A further complication in the task of discriminating brain damaged from schizophrenic patients is that of the nature of the brain damaged subjects. Organicity cannot be considered as a unitary entity any more than schizophrenia. Different types of brain damage will produce very different functional impairments (e.g., acute versus chronic, diffuse versus focal, static versus progressive). Differences in brain damaged populations also impinges on the outcome of various studies. For example, patients who have focal damage compared to chronic schizophrenics may be easily discriminable. However, chronic, progressive brain damage patients compared to

chronic schizophrenics may not be particularly discriminable. We know so comparatively little about the brain that subject matching, at its best, is rather tentative.

Comprehensiveness of Tests. Given the complexity of the brain, it is to be expected that finding a reasonable way of tapping the infinity of functional abilities is a problem. Single tests or shorter batteries are likely to present a biased picture of impairment of functional abilities. In fact, this has occurred in our understanding of schizophrenia in that early research utilizing limited batteries of tests rendered the erroneous conclusion that schizophrenics were characterized by damage to the frontal part of the dominant hemisphere only (Flor-Henry, 1976; Gruzelier and Hammond, 1976). More recently, there has been growing evidence that there is actually bilateral impairment to frontotemporal regions of the brain with greater impairment being found in the left hemisphere (Rochford, Detre, et. al., 1970; Watson, Thomas, Andersen, et. al., 1968; DeWolf, Barrell, et. al., 1971). Procedures not providing comprehensive assessment may, in this way, lead to erroneous conclusions. To-date, the most comprehensive battery in use for the purpose of assessing brain-behavior relationships is considered to be the HRNTB

(Golden, 1977).

Method of Analysis. According to Purisch, Golden and Hammeke (1978) global measures representing overall test performance and global quantitative comparisons can result in loss of valuable diagnostic information. Diagnostic accuracy can effectively be improved by going beyond these global measures (Lezak, 1976; Goldstein and Neuringer, 1966; Matarazzo, 1972). Qualitative analyses in each of these studies contributed significantly to improving diagnostic accuracy.

Medication Effects. Finally, the effects of medications are another factor which must be considered as potential contributors to the outcome of neuropsychological testing. Neuroleptic medications are well known for the extrapyramidal symptoms they produce as side effects to treatment (Andreasen, 1984). These drugs directly influence neurochemistry and consequently can be expected to alter the functional abilities of patients. In considering the influence of medications on neuropsychological test performance, it can be assumed, therefore, that functional abilities may be enhanced under the influence of medications that are within the therapeutic range and working effectively. This might be

expected to be true in the case of disorders which are neurochemical in origin. However, it is clear that some schizophrenics do not respond to these medications and the effect on their test performance may be less clear. In addition, recent changes in medications and/or administrations of medications which produce extrapyramidal symptoms may adversely affect test performance, clouding the interpretation of results. Assessing medication free subjects is likely to be the best means of eliminating this confounding variable. However, since it is not always practical to do this, Heaton et. al. (1979) suggest some guidelines to use when considering the effects of medication which will minimize confounding influences: (1) record the dosages of antipsychotic medications administered to each patient and check for significant group differences; (2) ensure testing is conducted well after the commencement or change of medications to assure the patient's adjustment to medication (e.g., when side-effects do not appear to be pronounced); (3) formally rate extrapyramidal signs prior to testing to rule out the presence of obvious adverse symptoms which may interfere with test performance.

Summary of Factors. In summary, there are many factors which appear to have contributed to the

inconsistency of findings regarding schizophrenic and brain damaged subjects which will need to be considered as part of future research. Chronicity seems to be the largest contributor to the inconsistency of results with a greater degree of impairment of brain functions being found among chronic schizophrenic patients than among fairly recent onset patients. Some discussion of the nature of the organic subjects as well points to the need to make groups under study as homogeneous and well matched as is possible. Other factors that emerge in the literature which may need to be considered as potential influences to outcome include: (1) assessing functional skills in a comprehensive manner so as to limit the change of biasing or drawing erroneous conclusions; (2) analysing the data through both quantitative and qualitative means to reduce the loss of valuable diagnostic information; (3) and eliminating, where possible, the confounding effects of medications.

C. Structural Brain Abnormalities in Schizophrenia

(a) Introduction

Identifying the link between "structures" of the brain and the "functions" they subserve has been an ongoing topic of study. Since Kraepelin's original view of schizophrenia as a disease of the brain, researchers have

been exploring the structural or organic attributes associated with the functional expressions of this illness. The following section is a review of literature pertaining to the identification of structural brain abnormalities that coexist with clinical manifestations of disturbed functioning in schizophrenia. Firstly, normal brain characteristics are discussed including a description of the physical structure and corresponding specializations of existing asymmetrical morphology of the normal brain (e.g., brain-behavior relationship). Secondly, literature pertaining to abnormalities present in schizophrenics' brains will be presented with respect to: (1) gross structural abnormalities as revealed through such measures as CT Scan (e.g., ventricular enlargement, atrophy); (2) abnormalities in cerebral lateralization (e.g., left hemispheric dysfunction); (3) metabolic abnormalities (e.g., changes in blood flow to various parts of the cerebral cortex). Finally, all of these topics are discussed with reference to various theories about the etiology they imply.

(b) Functional "Specialties" of Lateralized Asymmetries of the Brain

Normal Brain Morphology. The normal brain is

characterized by morphological cerebral asymmetries, as revealed by computerized tomographic scans (CT Scan) of the brain (LeMay, 1976). Specifically, normal asymmetry reveals that right-handed individuals tend to have wider right frontal and left occipital areas in their right hemisphere as compared to the respective contra-lateral structures of the left hemisphere. Left-handed individuals' pattern of asymmetry tends to be less striking, but nonetheless typically present (Galaburda, A. M., LeMay, M., Kempertl, et. al., 1978).

Functional Specialization. These asymmetries are now widely recognized as bearing a distinctive relationship to the functional "specialties" of different areas of the brain. For example, it is now widely accepted that the left cerebral hemisphere is specialized for language as well as abstract, sequential, and symbolic thinking, analytic processing, temporal analysis, detailed feature detection, linguistic and phonetic analysis; the right is specialized for visual spatial functions and more holistic processing as well as depth perception, line orientation, and rapid scanning of material (Kolb, et. al., 1980; Golden, et. al., 1981; Wexler, B. E., 1980). Normal cerebral lateralization is thought to evolve as part of the early developmental process.

(c) Abnormal CT Scan Findings and Associated Functional Deficits

Structural Abnormalities. There is a plethora of evidence detailing structural brain abnormalities present among schizophrenics. On the basis of these findings many hypotheses have been generated regarding etiological factors and pathogenesis of the disorder. Included in the "structural" abnormalities, ventricular enlargements (Golden, et. al., 1980; Weinberger, et. al., 1980; Pearlson, et. al., 1985; Andreasen, et. al., 1982; Kling et. al., 1983; Owens, et. al., 1985; Romani, et. al., 1986; Turner, et. al., 1986; DeLisi, et. al., 1986; Brown, et. al., 1986), reversals of presumed normal asymmetries (Tasi, Luke Y., Henry A. Nasrallah, Charles G. Jacoby, 1983; Largen, John W., Marcos Calderon, and Robert C. Smith, 1983; Golden et. al., 1981; Losonczy, et. al., 1986), and brain atrophy (Golden, et. al., 1980; Andreasen, et. al., 1986) have been substantially documented. There is no shortage of evidence that morphological abnormalities are present in some schizophrenics' brains. A fairly large sample of postmortem brains of schizophrenics (41), Brown et. al. (1986) confirmed that the ventricular enlargements hypothesized from CT scan evidence do in fact exist in a significant number of schizophrenic brains. The authors

further suggested on the basis of the finding of lower brain weight that such enlargement may be due to tissue loss, particularly to the left temporal lobe.

Functional Abnormalities. Similarly, many "functional" abnormalities have been documented as coexisting with these various morphological abnormalities. Language and cognitive impairments abound (Tsai, et. al., 1983; Scottish Schizophrenia Research Group, 1987), poor neuropsychological functioning (Golden et. al., 1980), a "negative" symptom pattern (Boronow, et. al., 1985; Andreasen, et. al., 1982), poor early premorbid adjustment (Pearlson, et. al., 1985; Guy, Liaboe, Wallace, 1986), early age of onset, poor response to neuroleptic treatment (Pearlson, et. al., 1985), limited social network (Seidman, et. al., 1987) and poor prognosis (Weinberger, et. al., 1980) are all factors associated with the schizophrenic syndrome.

Theories Integrating Structure and Function. While it is becoming apparent that there are subgroups of schizophrenics who suffer brain pathology (although it is also important to note that not all schizophrenics suffer brain damage), it is not clear to what this is attributable. Speculation about causality includes

theories regarding genetic predispositions (Woods and Wolf, 1983; Golden et. al., 1981) environmental assaults (e.g., viral infections, prenatal and perinatal complications such as asphyxia, head injury or predisposition to toxins) (Pearlson, et. al., 1985; Golden et. al., 1981; Andreasen, et. al., 1982), and degenerative progressive neuronal disease (Dewan et. al., 1983; Andreasen, et. al., 1986; Solomon, et. al., 1987). Convincing evidence for all of these hypotheses exists, leading to the inevitable conclusion of the likelihood of a multiplicity of causal agents producing a multiplicity of disease entities we collectively call schizophrenia.

In one interesting study, Woods and Wolf (1983) explored several factors purported to be determinants of ventricular enlargement. Reviewing a number of studies, the authors were able to determine that both a genetic influence and a specific environmental influence were factors involved. Based on their review of these studies, they hypothesized a genetic predisposition interacting with an environmental insult to the brain, resulting in the threshold for the clinical expression of schizophrenia being reached.

Their cogent argument was based on evidence drawn

from twin studies. Identical twins, discordant for schizophrenia were found to be differentiated by enlarged ventricles. Given the identical genetic inheritance of monozygotic twins, the brain abnormality and presence of schizophrenic symptoms was taken to be caused by a specific environmental brain insult afflicting one twin and not the other. Thus, a non-progressive environmental component was postulated.

Adding to this evidence, Woods and Wolf (1983) also observed a relationship between duration of illness and presence of ventricular enlargement: the longer the duration, the greater the likelihood of ventricular enlargement. This has been interpreted as evidence of a genetic unfolding of an inherited disorder which ultimately leads to a neuronal degenerative process (analogous to Huntington's Disease). This genetic determinant is said to predispose to the development of schizophrenia by involving certain critical neuro-structures and incidentally result in progressive ventricular enlargement due to tissue loss. Similarly, in a comprehensive study of chronic schizophrenic patients, Dewan, et. al. (1986) found both increased ventricles and densities of brain structures. They hypothesized that a pathological process may cause retraction of the ventricles and increased density. It is

also important to note here that although ventricular enlargement appears to increase progressively with duration of the illness, it is present from the outset and appears to predate the onset of acute illness (Weinberger et. al., 1982; Schulz, et. al., 1983; Llandrich et. al., 1986). Ventricular enlargement appears to both predate acute onset and progress during the illness. Evidence of greater CNS compromise early in development is also suggested by Green, Satz, et. al. (1987) on the basis of their finding of a greater incidence of minor physical anomalies among schizophrenics.

Evidence from other research on family factors also leads to the conclusion that genetics are an important determinant. For example, adopted-away offspring of schizophrenic patients have been found to be significantly more disordered than controls (Lowing et. al., 1983) and a higher incidence of the disorder is present in biological relatives of schizophrenic patients (Kety, 1983; Baron, et. al., 1985; Kendler and Hays, 1982).

Consistent with this hypothesis, a greater incidence of abnormal EEG findings (Kendler and Hays, 1982) and abnormal CT Scans (Romani, et. al., 1987; Owens, et. al., 1985) in schizophrenics for whom no significant

familial history was present was interpreted by these researchers as suggestive of brain dysfunction that has resulted from some environmental insult such as perinatal complications or subclinical viral infections. In contrast, normal EEG and CT Scans were found among schizophrenics with a high incidence of affected first degree relatives. A genetic etiological factor was hypothesized by these authors (Woods and Wolf, 1983) is that both genetic and environmental components may be necessary for the expression of schizophrenia to be manifested. Accordingly, based on twin studies, identical twins, discordant for schizophrenia are twin pairs in whom the postulated genetically-determined degenerative process alone has not been severe enough to lead to schizophrenia; it is only in the presence of the superimposed brain insult (non-progressive environmental component) suffered by one twin that the illness emerges. Pearlson, et. al. (1985) share this conclusion (e.g., interaction between brain damage, genetic predisposition and environmental stresses), having found a clear association between perinatal brain injury and ventricular enlargement in their study of schizophrenic patients. Head injury and perinatal complications, especially head injury or asphyxia are often associated with the onset of schizophrenia in adult life (Garmezy, 1978; Kety, 1980; Kinney and Jacobsen, 1978). It

has also been found that brain atrophy of schizophrenic patients is associated with worse premorbid functioning, particularly in childhood, (Weinberger, et. al., 1980; Nyback, H., et. al., 1982) and poor outcome (Delisi, et. al., 1983). Again, this implicates a neuropathological process occurring early in development for some schizophrenics.

A further step in exploring this evidence of genetic and environmental causal agents has resulted in the development of two theoretical models that incorporate the simultaneous contributions of genetic and environmental factors; the "additive" model and the "interactive" model. For example, Reveley, et. al. (1984) found a negative correlation between ventricular enlargement in schizophrenic patients and familial prevalence of schizophrenia (e.g., those with enlarged ventricles tended to have a negative family history for the disorder). This observation was interpreted in terms of an "additive" model of genetic (family prevalence) and environmental (enlarged ventricles) etiological factors and is supported by other researchers (Kendler and Eaves, 1986; Murray, et. al., 1985; Woods, Kinney, Yurgelun-Todd, 1986). It is hypothesized that the stronger the genetic liability, the less need for contributing environmental insults in order

for the expression of schizophrenic symptoms to occur.

Alternatively, Woods, et. al. (1987) suggest an "interactive" model based on their findings of increased prevalence of neurological abnormalities in families of schizophrenics for whom there was a positive history of affected first degree relatives. (Such neurological abnormalities have also been found in nonaffected family members of schizophrenics by Kinney, Woods and Yurgelun-Todd, 1986). In effect, the genetic predisposition (family prevalence of illness) coupled with the environmental insult (prevalence of neurological signs among family members) is hypothesized to interact exponentially, predicting increased familial prevalence of illness in members exposed to the environmental factor.

The preceding has suggested a hypothesis regarding the general brain pathology found to be present in some schizophrenics based on the enlargement of ventricles and atrophy shown on CT Scans. A body of literature exists more specifically implicating a primary site of deficit occurs in the left hemisphere, most notably in the anterior area (Luchins, et. al., 1979, 1982; Andreasen, et. al., 1982; Golden, et. al., 1981; Coffman, et. al., 1984).

For example, Coffman, et. al., (1984) revealed an overall decrease in relative density of the left hemisphere (decreased density is used to predict cell loss or atrophy) in his sample of schizophrenic subjects, with density deficits in frontal regions as well as parietal and occipital regions; similarly, Benes, et. al. (1986) found decreased neuron density in the prefontal and motor cortexes; Kling, et. al. (1983) revealed an absence or reversal of the usually expected frontal asymmetry; Tsai, et. al. (1983) found a higher frequency of reversed occipital asymmetry; density measures of Golden, et. al. (1981) localized the primary area of deficit to the anterior area of the left hemisphere; Luchins, et. al. (1982) revealed reversals in normal asymmetry, with two distinct groups being apparent: one with generalized atrophy and another with reversed asymmetry. Genetic and environmental hypotheses are variously argued as predictive of these findings.

D. Cerebral Lateralization Abnormalities

(a) Introduction

The process of cerebral lateralization is thought to occur very early in development and consequently, reversals in cerebral asymmetries in the absence of more

general atrophy is taken as evidence in support of a theory of genetic predisposition (Luchins, et. al., 1982). This abnormal laterality appears to interfere with normal language function, that is important in the pathology of schizophrenics according to findings that schizophrenics with reversed asymmetry also obtained lower Verbal I.Q. scores (Luchins, et. al., 1982).

Additionally, decreases in density, emphasized in the left hemisphere are postulated to result from brain insult inhibiting proper growth of the left frontal hemisphere (Golden, et. al., 1981; Dewan, et. al., 1983; Andreasen, et. al., 1986). Luchins', et. al. interpretation of their findings suggest that schizophrenics with cerebral atrophy may be hyperlateralized and those without atrophy (and reversed or absence of normal asymmetries) may be hypolateralized. Distinct left hemispheric hypofunctioning with compensatory right hemispheric overactivation has been observed in some schizophrenic patients (predominantly in sensorimotor areas during dominant hand motor tasks) (Guenther, Breitling, et. al., 1986). In any event, the normal "specialized" functions of the hemispheres are impaired and the absence of differences in density of left-right values, or abnormalities of activation of cerebral activation may be

due to an increase in right hemispheric values or a diminuation of left hemispheric values (Coffman, et. al., 1984).

The view of left hemispheric dysfunction for schizophrenics has emerged predominantly on the basis of studies of cerebral lateralization. Essentially, three different views prevail with regard to hemispheric lateralization of schizophrenics: (1) schizophrenics have a lateralized left hemispheric dysfunction; (2) they have a dysfunction of inter-hemispheric transfer; (3) they have reversed asymmetry or diminished asymmetry, complicating and hampering normal cerebral specializations (Merrin, 1981). Following is a review of literature pertaining to the first two of these hypotheses (the latter having already been discussed in the previous section).

(b) Left Hemispheric Dysfunction

Included among the findings in support of left hemispheric dysfunction is a higher incidence of sinistrality in schizophrenic patients as compared to controls (Gur, 1977; Nasralah, et. al., 1981); in monozygotic twins, discordant for schizophrenia and handedness, the schizophrenic twin is more likely to be

left-handed (Boklage, 1977); a preponderance of right lateral eye movements in response to cognitive operations (implying overuse of the left-hemisphere) (Gur, 1978); defects in ocular-motor subsystems (e.g., visual information processing requiring sensory perceptual and motor functions) (Mather and Putchat, 1983; Piran, Bigler and Cohen, 1982; Schwartz, McGinn and Winstead, 1987); poor eye tracking (Solomon, et. al., 1987); a greater number of left hemisphere errors on neuropsychological tests (e.g., lower Verbal I.Q., more left hemispheric errors on Aphasia Screening Test) (Flor-Henry, 1976; Gruzelier and Hammond, 1979; Taylor, et. al., 1979); reduced cerebral blood flow to left frontal and occipital areas of the brain (Ingvar and Franzen, 1974); widespread left-hemispheric dysfunction as evidenced from EEG mapping (Guenther, Brietling, Banquet, et. al., 1986).

Generally, when one part of the brain undertakes a function that is ordinarily a specialty of another part, it is indicative of a deficit in the area in which the function is normally handled most effectively (Schweitzer, 1982). It may be inferred then that the phenomenon of a preponderance of left-handedness among schizophrenic patients is associated with early organic factors such as perinatal hypoxia or subclinical viral infections. This

could conceivably create a weakening of the normal left hemispheric dominance and result in a shift from normal laterality, manifested by a consequent shift to left-handedness which is controlled by the contra-lateral right hemisphere (Nasrallah, et. al., 1981). It has been ascertained that there is hyperarousal or overactivation in parts of the left hemisphere for some schizophrenic patients (Newlin, et. al., 1981; Schweitzer, 1978, 1982; Gur, 1978; Erlichman and Weinberger, 1978; Alpert, et. al., 1976; Bahzin, et. al., 1975; Torrey, 1980). In effect, it appears as though the left-hemisphere is overactive in undertaking functions such as spatial detection that are normally most effectively handled by the right hemisphere.

The ordinarily preferred right hemispheric processing of spatial material is thought to result in concomitant inhibition of the left hemisphere for this function. This does not appear to occur for many schizophrenics. Consequently, Schweitzer (1982) hypothesized this failure of the right hemisphere to preferentially select this information and simultaneously inhibit the left hemisphere may lead to an overload to the left hemisphere (which typically is designed for smaller, sequential processing) and may give rise to secondary attentional deficits, general impairment of information

processing, and interference of left hemispheric deductive, linguistic and step-wise information processing. It makes sense that the left hemisphere would be inclined to be more easily overloaded with information, given its sequential, step-wise style of processing, compared to the rapid scanning, holistic style of the right hemisphere. The left is, therefore, assumed to have a more limited capacity (Tomer, et. al., 1981) and when called upon to process large amounts of information conceivably could be prone to overload and thus falter. The cognitive and language deficits among schizophrenics may be explained in this manner.

Following this same theme of overload to a part of the brain resulting in inhibition of the normal capacity for information processing, misaligned pyramidal cells in the hippocampus area of schizophrenics' brains have been detected through a neurohistological study conducted by Kovelman and Scheibel (1984). Consistent alteration in pyramidal cell orientation was found to be present, most specifically located within the left hippocampi. An hypothesis drawn about these malpositioned cells is that they may alter normal patterns of synaptic linkage leading to disturbed information processing in the affected areas. A synaptically idiosyncratic hippocampus would undoubtedly

create an unreliable foundation from which to interpret the environment.

The authors believe it is unlikely that such an anomaly could develop at any time except embryogenesis when the cells are going through their developmental migratory process. The fact that no correlation between advancing age and degree of cell disorientation was found in this study supports the assumption that this anomaly occurs early in development.

(c) Interhemispheric Transfer Dysfunction

Information is communicated between the two hemispheres via the corpus callosum. Split-brain (e.g., disconnected corpus callosum) studies have yielded valuable information about the intercommunication of the right and left hemispheres. Left-hand anomia is considered to be one of the classical signs of a split-brain. Dimond, et. al. (1979) assessed schizophrenics using one of the split-brain tasks. Objects put into the left hand (operated by the right hemisphere) of split-brain individuals cannot be named. Naming takes place in the left hemisphere and the information about the feel of the objects cannot be transferred to the left under the condition of

split-brain; the transfer mechanism (corpus collasum) is inoperative. Schizophrenics made a significantly higher number of left-handed errors on this task and this was interpreted by the authors not so much as the classical anomia of the split condition, but more as a "noisy communication channel which cannot always be relied upon to convey the correct message."

Additionally, enlarged corpus callosums in schizophrenics, unrelated to age (Rosenthal and Bigelow, 1972) and poor performance of schizophrenics on bimanual tactual tasks (performance of bimanual coordination is said to be subserved by the left frontal hemisphere) (Green, 1978; Carr, 1980) have been found to occur more frequently in schizophrenic patients. Difficulty with interhemispheric transfer of information has been hypothesized on the basis of these data. The fact that these abnormalities appear unrelated to age suggests a preexisting developmental disorder rather than a degenerative disorder (Golden, et. al., 1980). A more recent study (Merriam and Gardner, 1987) revealed that this pattern of better intrahemisphere than interhemisphere processing exists in normals as well as schizophrenics, but that schizophrenics are generally less efficient at both types of processing. This was interpreted as evidence that

schizophrenics do not show an interhemispheric dysfunction specifically.

E. Metabolic Abnormalities

(a) Introduction

Metabolic abnormalities found among schizophrenics confirm the hypothesis of left-hemispheric overactivation. These abnormalities are ascertained primarily on the basis of studies regarding cerebral blood flow (CBF). The flow of blood to the cerebral cortex has been shown to increase during the performance of motor, sensory and cognitive activity, and CBF measures are thereby used to assess cortical activation in various parts of the brain as it relates to brain-behavior functions (Gur, et. al., 1983). The following review of studies pertain to illucidating abnormal findings with regard to the CBF of schizophrenic patients.

(b) Abnormal Patterns of Cerebral Blood Flow (CBF)

There appear to be two distinct patterns of abnormal CBF among schizophrenics namely, one of whole brain blood flow and one of more localized changes. In the first pattern some schizophrenic subtypes appear to have

higher whole brain blood flow, while in other subtypes a pattern of lower whole brain blood flow is characteristic (Gur, Resnick, Alvani, et. al., 1987). The presence of the pattern of higher CBF has been associated with the presence of "productive" symptoms (e.g., "positive", florid symptoms), and the lower whole brain CBF with "nonproductive" symptoms (e.g., "negative", defect symptoms) (Hoyer and Oesterreich, 1975). Guenther, Moses, Meuller-Spahn, et. al. (1986), for example, found bilateral hyperflow and diffuse cortical flow increase for Type 1 (positive symptom) schizophrenics. Widespread nonreactivity of CBF was found for Type II (negative symptom) schizophrenics.

A second pattern suggests localization of CBF changes. For example, greater accentuation CBF increase to the left hemisphere, particularly the left frontal region has been detected (Ariel, et. al., 1983; Gur, et. al., 1983; Gur, et. al., 1985; Mathew, et. al., 1981; Weinberger, Berman and Zec, 1986). This is generally regarded as evidence in support of the left hemispheric overactivation theory. Additionally, abnormal lateral processing is inferred on the basis of the fact that schizophrenics, in contrast to normals, demonstrate increased CBF to the left hemisphere during spatial tasks

and no change in CBF during verbal tasks. Cerebral blood flow, for normal individuals increases in the right hemisphere for spatial tasks and increases in the left hemisphere during verbal tasks (Gur, et. al., 1983; Gur, et. al., 1985, 1987). Finally, low severity groups of schizophrenics showed more specifically localized CBF changes to the anterior regions of the left hemisphere; high severity groups, in contrast, were more likely to show abnormal activation of flows to both anterior and posterior areas of the brain (Gur, et. al., 1985).

F. Neuropsychological Abnormalities

A variety of neuropsychological test batteries are utilized in the assessment of brain functions. Among the most frequently used, of course are the HRNTB and Luria-Nebraska Neuropsychological Test Battery. However, other batteries often are constructed by researchers to assess, for example, functioning in specific areas of the brain. Despite the variety of batteries used, a remarkable consistency of findings in the assessment of schizophrenics is beginning to emerge as is illustrated by the following.

(a) Discriminative Power of Neuropsychological Tests

A number of studies of neuropsychological functioning of schizophrenics have been expressly aimed at the discriminative power of these tests (Watson, Thomas and Felling, 1968; Levine and Fierstein, 1972; Lewis, Nelson and Eggersten, 1979; Heaton, et. al., 1979; Purisch, Golden and Hammeke, 1978; Watson, Thomas, Felling and Anderson, 1969). In these studies comprehensive neuropsychological batteries such as the HRNTB were used with schizophrenic, brain damaged patients and control subjects, but subject groups tyically were heterogeneous and discussion of results limited to the discriminitive efficacy of neuropsychological tests. In the Watson, et. al. (1968) study using chronic schizophrenic patients (e.g., 73 months hospitalization), Category Test results classified 84% of the schizophrenics as brain damaged; the Tactual Performance Test classified 80% as brain damaged; the Seashore Rhythm Test 74%; Speech Sounds Perception Test 80%; Finger Tapping Test 50%. The authors noted that the Impairment Index would likely result in the classification of long-term patients as organic and short-term as schizophrenic. Recent onset schizophrenics were classified as brain damaged 76% of the time and the chronic patients were classified as brain damaged 92% of the time. The main outcome of this type of study is that many schizophrenics appear to function much like brain damaged individuals.

(b) Functional Impairments in Schizophrenia

More recently, however, neuropsychological research efforts have been directed towards the description of functional impairments of schizophrenics on the basis of more homogeneous subgroupings (Guy, Liaboe, Wallace, 1986; Nyman, et. al., 1986; Robertson and Taylor, 1985; Opler, et. al., 1984; Green and Walker, 1984; Nyman, et. al., 1986). Often, however, limited batteries of cognitive measures are used or heterogeneous groupings of schizophrenics are studied. For example, neuropsychological batteries have been limited to such tests as: the Wechsler-Bellevue Intelligence Scale (Nyman, et. al., 1986); the WAIS, plus a verbal fluency, visual retention and visual recognition test (Robertson and Taylor, 1985); Memory for Designs, Benton Visual Retention Test, Trail Making Test and Vocabulary Subtest of the WAIS (Guy, Liaboe and Wallace, 1986). Negative symptom schizophrenics have been found to display more primitive cognitive modes and greater psychomotor retardation (Opler, et. al., 1984) and significantly slower information processing than positive symptom patients (Green and Walker, 1984). In general, results from these studies unequivocally indicate that schizophrenic subjects perform more poorly on cognitive tasks than control subjects.

In one of these studies (Robertson and Taylor, 1985) symptom patterns were compared with cognitive deficit profiles. Four separate symptom groups emerged from their analysis of symptoms ("deluded" - history of delusions; "mixed symptom" - full range of positive and negative symptoms; "simple" - insidious onset/negative symptoms; "atypical" - high anxiety/obsessionality), with each group being characterized by different cognitive deficit patterns ("deluded" - short-term memory/perception of verbal/non-verbal material deficits; "mixed" - impaired integration of verbal/nonverbal material; "simple" - impaired searching ability from stored material; grossly impaired higher order conceptualization; "atypical" - impaired concentration). The fact that different cognitive deficit profiles emerged for the clinically distinct symptom patterns was interpreted by the authors as evidence in support of the notion of different illnesses. Unfortunately, the battery of tests used in this study was limited and thus so were the descriptive deficit profiles. There are very few such studies that systematically explore both symptom patterns and cognitive deficit patterns in a comprehensive manner.

Similarly, Chelune, et. al. (1979) examined the level versus pattern of neuropsychological performance

among schizophrenic and diffusely brain-damaged patients. Results of level of performance scores and deficit pattern analysis scores for a heterogeneous grouping of schizophrenic patients were compared with a brain-damaged group. Again, the intent was directed at discriminating the schizophrenic from the brain-damaged group. Findings revealed it was possible to distinguish between the groups on the basis of mean level of performance of neuropsychological tests (diffusely brain-damaged patients did more poorly on the brain-sensitive measures). However, the deficit patterns did not differ significantly between groups. Homogeneous subgroupings of schizophrenics may have produced different results.

(c) Inferred Localization of Deficits

Research efforts have also been directed towards linking the functional deficits to brain structure and hypothesized etiologies (Taylor and Abrams, 1984; Flor-Henry, 1976; Gruzelier and Hammond, 1976; Kolb and Whishaw, 1983; Wexler, 1980). Taylor and Abrams (1984) conducted a comprehensive study to assess the cognitive functioning of 62 schizophrenics using several neuropsychological tasks. Approximately three-quarters of their schizophrenic subjects, who had been rigorously

defined, exhibited moderate to severe cognitive impairment. This impairment was described by the authors as being bilateral diffuse impairment occurring in the anterior fronto-temporal regions of the brain. Further, the impairment appeared most pronounced in the dominant left hemisphere.

A prevalent notion about schizophrenia, as has been referred to previously, is that impairment exists exclusively or primarily in the dominant hemisphere (Flor-Henry, 1976; Gruzelier and Hammond, 1976; Nyman, et. al., 1986). Taylor and Abrams' results are at variance with this. It appears to be the case, however, that studies by investigators who use a battery of tests such as the HRNTB or Luria-Nebraska are more likely to find profound bilateral dysfunction (Taylor, Redfield and Abrams, 1981; Abrams, Redfield and Taylor, 1981; Silverstein and Meltzer, 1983), whereas those who use single tests are more likely to report unilateral dominant hemisphere dysfunction (Beaumont and Dimond, 1973; Gur, 1978, 1979; Connolly, Gruzelier, Kleinman, et. al., 1979).

Silverstein and Zerwic (1985) also infer frontal lobe pathology from findings obtained in their study. A group of 18 neuropsychologically impaired and 30

neuropsychologically intact schizophrenics were further assessed for psychotic symptomatology. Neuropsychological impairment was determined on the basis of the degree of correspondence between the Luria-Nebraska scales and CT Scan abnormality (enlarged ventricles). Impaired schizophrenics demonstrate a lower prevalence of delusions of reference and persecution. The lower incidence of these paranoid symptoms in impaired patients was hypothesized to be attributable to a less coherent or less well integrated clinical picture. In turn, this was considered to stem from the neuropsychological dysfunction. The impaired group did not have the functional abilities to contrive a well organized delusional system.

A diminished capacity for insight was also discovered by Silverstein and Zerwic (1985) among the impaired group compared to the intact group. This was interpreted by the authors as suggestive of anterior frontal cortex dysfunction due to deficits in planning, organizational and evaluative functions which are central to the overall integration of behavior conducted in the frontal regions.

Bilateral dysfunction of the frontal and temporal lobes in schizophrenics has also been inferred by Kolb and

Whishaw (1983) who, in their study, specifically assessed frontal, temporal and parietal lobe functioning of their patients using several different tests for each lobe. Specific tests were chosen to reflect the functional status of the left frontal lobe (e.g., Wisconsin Card Sorting, Semmes Body Placing Test, Chicago Word Fluency), right frontal lobe (Gotman Design Fluency), left temporal lobe (Delayed Recall - Wechsler Stories and Paired Associates, Dichotic Listening, Newcombe Word Fluency), right parietal lobe (Rey Complex Figure Copy, Corsi Block Span, Mooney Closure Test). Schizophrenic patients performed very poorly, compared to a matched control group, on tests sensitive to the left or right parietal lobe function.

The authors conclude that although the "left-for-schizophrenia" theory has become popularized over the past few years it is not supported by their findings. In fact, Wexler (1980), in a recent review of the literature in this regard also found there is no substantiation for the "left-for-schizophrenia" theory evident in the general body of psychological literature.

(d) Summary of Deficits

In summary, the efficacy of neuropsychological

assessment of schizophrenics has been established and neuropsychological test data converge with data from other sources such as CT scan, metabolic studies and EEG confirming the unequivocal conclusion that some schizophrenics are brain impaired. Schizophrenics do poorly on cognitive tasks and findings have been interpreted as evidence of bilateral fronto-temporal involvement. Consistency of these results occur from a variety of sources and types of data. Different neuropsychological test batteries have been used by different researchers yielding the same results, so it is unlikely to be an artifact of any specific test battery (Marvel, Golden and Hammeke, 1979; Goldstein and Halperin, 1977; Flor-Henry and Yeudall, 1979). Physiological measures also identify greater anterior dysfunction in schizophrenia (Ariel, Golden, Berg, et. al., 1983; Gruzelier and Venables, 1974; Ingvar and Franzen, 1974).

The dominant fronto-temporal accentuation may, however, reflect the specific diagnostic criteria used in these studies, according to Taylor and Abrams. As mentioned previously, over the past twenty years schizophrenia has become defined on the basis of the presence of the more florid (positive) symptoms of schizophrenia. It may well be that this group of

schizophrenics in particular exhibit fronto-temporal dysfunction which is more prominent in the left hemisphere. Alternatively, the finding of bilateral impairment that is of a diffuse nature may relate to the original classification of schizophrenia as a dementia. There is evidence that different symptom patterns are associated with different cognitive deficit profiles (Robertson and Taylor, 1985). These differences may reflect different disease processes.

G. Summary and Synthesis of Review of Literature

In this chapter, a review of literature pertaining to brain functioning of schizophrenics has been presented incorporating research from a diversity of areas including results from CT scans measuring gross anatomical brain structures and studies detailing abnormalities of lateralization and cerebral metabolism, as well as neuropsychological assessment of adaptive functioning. A convergence of evidence from this variety of sources yields the unequivocal conclusion that brain pathology exists among many schizophrenics. Impairments in language, cognitive and other adaptive functions have been found to be associated with structural abnormalities such as enlarged ventricles, cerebral atrophy, reversals or

absences of the normal asymmetry of the brain, changes in cerebral blood flow, and pyramidal cell abnormalities. This consistency of data is strong evidence converging toward the conclusion of brain pathology among schizophrenics.

A dichotomous clustering of symptoms has been consistently found in clinical descriptions of the schizophrenic syndrome. "Productive" florid symptoms contrast with a "defect", "nonproductive" clustering of symptoms, originating from Kraepelin's and Bleuler's initial descriptions of schizophrenia. More recently, Andreasen and Crow support this division, in the theories they offer with respect to the etiology and pathogenesis of schizophrenia.

In the preceding review of literature, such distinctions were made about the nature of schizophrenic brain pathology. For example, in studies utilizing CBF measures, two distinct groups emerged. (1) In the first one, the whole brain was affected with either an increase or a decrease in blood flow. Whole brain increases tended to be associated with "productive" symptoms and whole brain decreases with "nonproductive" symptoms. (2) In the second group, only specific areas of the brain were affected. A

pattern of left anterior (associated with low severity) or left anterior and posterior (associated with high severity) changes in CBF existed. CT scan results similarly reveal different patterns of pathology. (1) Some schizophrenics reveal general brain atrophy (perhaps analygous to the whole brain changes of CBF). Brain insult was postulated as the etiology of these abnormalities. (2) Alternatively, reversals in asymmetry typically occurred in the absence of atrophy and a genetic influence was interpreted as causal in this instance. Finally, abnormal EEG patterns appear to exist in schizophrenics for whom no positive family history was reported. This led to the hypothesis of brain insult being the important etiological component. A group of schizophrenics with normal EEG's have a strong positive family history, with many first degree relatives being afflicted with schizophrenia also. A genetic component was hypothesized as being the important causal agent. Neuropsychological data similarly provide evidence of impaired adaptive functioning in some schizophrenics. In addition, within this impaired group some very minimal data is beginning to emerge reflecting that different cognitive deficit profiles can be linked to different symptoms patterns, thereby implying the possibility of distinctly separate underlying etiological processes.

It seems clear then that different patterns of brain pathology, associated with different functional expressions exist among schizophrenics. These different manifestations are theorized to reflect different disease entities and warrant further investigation (Crow, 1980; Andreasen, 1982).

CHAPTER IV

RESEARCH PLANS AND METHODS

A. Introduction

The proposition that schizophrenic symptoms can be divided into the two categories of positive and negative symptoms was first put forth by Hughling-Jackson (1931). Despite the fairly long-standing existence of this concept, research applications of the idea have been limited due to the lack of reliable methods of assessing negative and positive symptoms (Kulhara, Kota and Joseph, 1986). Efforts to group schizophrenics on the basis of these symptoms have thus been impeded. More recently, the concept of positive and negative symptoms has undergone study for the purpose of assessing validity of the construct and reliability of its measurement. The outcome of these studies has resulted in the development of more sensitive and reliable instruments to assess these symptoms (Andreasen, 1981; 1984; Lewine, Fogg, Meltzer, 1982), and their credibility has been established (Andreasen, 1982; Andreasen and Olsen, 1982; Allen, 1983; Lindenmayer and Opler, 1984; Johnstone, Owen, Frith and Crow, 1986; Kay, Fiszvein, Lindenmayer, Stanley and Opler, 1986). The

stability of differences found between positive and negative symptom schizophrenics across a four year period has lead Johnstone, Owens, Frith and Crow (1986) to suggest different pathological processes underlie these syndromes.

Until fairly recently also, the focus of research employing neuropsychological measures with a schizophrenic population has been aimed at determining the discriminitive power of tests to distinguish schizophrenia from brain damaged individuals. The growing body of evidence through such means as CT scan, EEG, metabolic measures, etc. provides an impressive convergence of data revealing a brain impaired subclass of schizophrenics. Golden (1983) suggests that within this context, neuropsychological tests may be used to "evaluate the interplay between neurologic and psychiatric factors in schizophrenia, rather than simply to rule out organicity in schizophrenic patients", and this is beginning to occur. To-date, neuropsychological assessment of schizophrenics has been characterized by an emphasis on the discriminative power of the tests; a tendency to assess heterogeneous groups of schizophrenics; a lack of comprehensiveness of assessment of neuropsychological functions (e.g., limited measures of cognitive functions); and limited analysis of qualitative information of tests.

Given the diversity of symptom clusters present in the literature on schizophrenia, it is likely that the heterogeneous group we call schizophrenia actually represents a multiplicity of different disease entities. In order to separate out specific disease entities to ultimately be able to identify the etiology of any one specific disorder, subgroupings with similar symptom patterns must be studied. The objective of this study was to assess schizophrenics on the basis of a meaningful subgrouping. The dichotomy of positive and negative symptom schizophrenics has emerged and persisted across time, and may serve as such a meaningful division. A further objective of this research project was to examine the neuropsychological test performance of subgroupings of schizophrenics to assess the possibility that different patterns of brain-behavior relationships may exist between groups, and thus reflect different patterns of abnormal cerebral functioning.

The number of subjects included in this study was relatively small due to rigorous inclusion criteria and availability of subjects. Although statistical analyses of data were conducted, it was assumed that usefulness of such statistics with the small number of subjects per subgrouping would be limited. The statistics conducted

were therefore used to facilitate the more descriptive intent of analysing the data so as not to lose the subtleties of patterning of performances between and within groups. In accordance with this more descriptive plan of analysis, research questions rather than hypotheses are presented in this chapter.

Determining whether or not specific significant differences exist between Positive, Negative and Mixed symptom schizophrenics in the neuropsychological deficits they exhibit on the Halstead-Reitan Neuropsychological Test Battery was an aim of this research project. When significant differences were determined, a further objective was to assess the specific patterning of neuropsychological deficits present within the parameters of Positive, Negative and Mixed subgroupings in order to foster a better understanding of the nature of brain-behavior relationships and brain deficits among schizophrenics.

B. Subjects

The subjects were selected from two inpatient hospital settings: Alberta Hospital Ponoka and Alberta Hospital Edmonton. Demographic data for the sample of

schizophrenic patients (N=53) is presented in Table 1. Seventy-four percent (74%) (N=39) of the sample were male and 26% (N=25) female. Subjects ranged in age from 19.92 to 62.17 years with a mean age of 33.37 years. Twenty-one percent (21%) of the sample were predominantly left-handed, while 79% were right-handed. The vast majority of subjects had attained an educational level of grade 10 or better (81%), with 41% having completed grade 10 to 12, 19% having attended a post-secondary vocational institution or college, and 21% having attended a post-secondary academic university. The remaining 19% of the subjects had achieved a lower than grade 10 educational level. Sixty-six percent (66%) of the sample had been single all their lives, 26% had been married or lived in a common-law arrangement, 8% were either separated or divorced. The mean duration of illness for the total sample was determined from their first psychiatric hospitalization to the date of assessment for this study. The mean duration of illness was 84.546 months or 7.039 years.

TABLE 1

Demographic Data
Number and Percent of Total Sample (N=53)

Variable	Nbr. of Ss	% of Total Sample
- Sex		
female	N=14	(26%)
male	N=39	(74%)
- Age		
Range	19.92 to 62.17 years	
Mean Age	33.3666 years	
- Lateral Dominance		
Right-handed	N=42	(79%)
Left-handed	N=11	(21%)
- Education		
K. to Gr. 9	N=10	(19%)
Gr. 10 - 12	N=22	(41%)
Vocat./College	N=10	(19%)
Univer/Academic	N=11	(21%)
- Marital Status		
Single	N=35	(66%)
Married/Comm. Law	N=14	(26%)
Separ./Divorced	N=04	(08%)
- Duration of Illness (from first psychiatric hosp.)		
Mean	84.462 mo. or 7.039 yr.	
Median	66.000 mo. or 5.500 yr.	

C. Procedure

Patients included in the study were psychiatrically diagnosed as schizophrenic. Given the inconsistency of diagnostic practices with respect to this disorder, to be reasonably assured of the reliability of diagnosis, subjects were chosen on the basis of having received a consistent diagnosis of schizophrenia throughout their clinical history. Patients used in this study had received a diagnosis of schizophrenia from no less than two psychiatrists and were currently admitted with a diagnosis of schizophrenia. Subjects for whom there was substantial equivocation about the diagnosis were excluded from the sample.

Conditions of data collection varied between the two institutions. There were differences in the completion of the symptom checklists (SAPS/SANS) and neuropsychological testing, as well as patient medication level at the time of testing. A total of 29 patients were medicated at the time of testing, and 24 were not. For 31 of the patients, symptom checklists (SAPS/SANS) were completed by staff members who were familiar with the patient's symptoms and thus able to rate their severity, while for 22 of the patients, symptom checklists were

completed from chart information by the researcher on the basis of whether the symptom was present or absent. This was necessary because these patients had been discharged from the hospital and were thus unavailable for direct assessment of symptoms. Symptom checklists were filled out primarily from four sources in the patient's chart ("Patient History" and "Discharge Summary" completed by physicians as well as those completed by the social worker which typically incorporated information from outside sources, usually family members). For 25 patients the HRNTB was completed by psychological technicians hired to conduct testing as part of this project; for 28 subjects this testing had already been completed for either clinical or other research purposes, and in these cases the preexisting information was obtained from the patient's chart to be included as part of the study. Table 2 contains a summary of these factors.

TABLE 2

Conditions of Data Collection

Nbr. of Ss	Location	Source of Information SAPS/SANS Symptom Checklist	HRNTB	Medic. Status
25	AH-Ponoka	Completed by staff	testing conducted as part of project	medic.
2	AH-Edm.	Completed by staff	conducted by AHE info from chart	medic.
4	AH-Edm.	Completed by staff	conducted by AHE info from chart	unmed.
2	AH-Edm.	obtained from chart	conducted by AHE info from chart	medic.
20	AH-Edm.	obtained from chart	conducted by AHE info from chart	unmed.
Total number of Ss medicated = 29 Total number of Ss unmedicated = 24				

Preset appointments were arranged with subjects in coordination with staff and psychological technicians. Assessment for each subject was conducted over a minimum of two separate sessions in order to avoid fatigue, although often the completion of testing took more than two sessions. In the event that a subject's tolerance for testing was low for any reason, technicians were instructed to discontinue and to break testing into shorter time periods as deemed necessary in order to facilitate adequate cooperation.

Patient compliance, cooperation, ability to follow instructions and sustain effort were stressed as essential to the validity and reliability of results. The following guidelines were provided for testing technicians in the event a subject appeared unable to meet these criteria at the time of contact:

(a) discontinue for the day;

(b) approach on another day and reattempt;

(c) if further attempts (approximately 2-3) continue to be met with resistance or inability to cooperate, discontinue testing.

D. Instruments

Assessment measures included the following:

(a) Assessment of Positive and Negative Symptoms

(i) Scale for Assessment of Positive Symptoms (SAPS). This scale contains items for rating thirty-four positive symptoms in schizophrenia, combined to form four global measures (hallucinations, delusions, bizarre behavior, positive formal thought disorder).

(ii) Scale for Assessment of Negative Symptoms (SANS). This scale contains items for rating thirty negative symptoms in schizophrenia, combined to form five global symptoms (alogia, affective flattening, avolition-apathy, anhedonia-asociality, and attentional impairment).

The global symptoms for both scales were empirically chosen. Reliability was assessed using an interrater reliability design with excellent results (.92). These scales have also been found to have good internal consistency (Andreasen, 1982).

TABLE 3

Assessment of Positive/Negative Symptoms
Total Scores and Global Ratings
Test Variables

Positive Symptoms

1. Hallucinations
2. Delusions
3. Bizarre Behavior
4. Positive Formal Thought Disorder

Negative Symptoms

1. Affective Flattening or Blunting
2. Alogia
3. Avolition - Apathy
4. Anhedonia - Asociality
5. Attention

The diagnostic criteria for Positive Schizophrenia are:

1. At least one of the following is a prominent part of the illness.

a. Severe hallucinations that dominate the clinical picture
b. Severe delusions

c. Marked positive formal thought disorder
d. Repeated instances of bizarre or disorganized behavior

2. None of the following is present to a marked degree.

a. Alogia
b. Affective flattening
c. Avolition-apathy
d. Anhedonia-asociality
e. Attentional impairment

Diagnostic criteria for Negative Schizophrenia are:

1. At least two of the following are present to a marked degree:

a. Alogia
b. Affective flattening
c. Anhedonia-asociality
d. Avolition-apathy
e. Attentional impairment

2. None of the following dominates the clinical picture or is present to a marked degree.

a. Hallucinations
b. Delusions
c. Positive formal thought disorder
d. Bizarre behavior

Criteria for Mixed Schizophrenia include those patients that do not meet criteria for either positive or

negative schizophrenia, or meet the criteria for both (Andreasen and Olsen, 1982).

Symptoms were considered to be 'marked' on the SAPS and SANS when a rating of at least 4 was given on the scale of 0 to 5. Appendix A and B contain a description of diagnostic criteria for each of the symptoms for the SAPS/SANS.

(b) Intellectual Testing - WAIS-R

The WAIS-R is an individually administered test. It was designed by its author to assess intelligence, defined as the "aggregate or global capacity of an individual to act purposefully, to think rationally, and to deal effectively with the environment" (Wechsler, 1944). The test is comprised of 11 subtests, from which three I.Q. scores (Verbal, Performance and Full Scale) can be derived. Reliability coefficients are .97 for the Verbal I.Q., .93 for the Performance I.Q. and .97 for the Full Scale I.Q. The norms are based on a sample of 1,880 adults ranging in age from 16 to 74 years, 11 months, stratified on the basis of age, sex, race, geographic location, occupation, education and urban-rural residence (Wechsler, 1981). The standardized mean I.Q. for this test is 100, with a

standard deviation of 10 and the mean score for individual subtests is 10 with a standard deviation of 3. Table 4 provides a list of test variables analysed from the WAIS-R for this study.

TABLE 4
Wechsler Adult Intelligence Scale - Revised
Test Variables

1. Verbal I.Q.	8. Comprehension
2. Performance I.Q.	9. Similarities
3. Full Scale I.Q.	10. Picture Completion
4. Information	11. Picture Arrangement
5. Digit Span	12. Block Design
6. Vocabulary	13. Object Assembly
7. Arithmetic	14. Digit Symbol

(c) Halstead-Reitan Neuropsychological Test Battery (HRNTB).

The HRNTB was developed through study of thousands of patients with known neurological disease or damage. Tests were developed to reflect brain-behavior relationships and have been continuously validated over many years on the basis of use in these cases where the area of damage or disease process was known. The battery

covers a broad range of functions performed by the brain and consists of several tests which fall into six categories: (1) input measures; (2) tests of attention, concentration and memory; (3) tests of verbal abilities; (4) measures of spatial, sequential and manipulatory abilities; (5) tests of abstraction, reasoning, logical analysis and concept formation; (6) output measures (Reitan, 1985).

Evaluation of the HRNTB results was conducted on the basis of four methods of inference: (1) Test scores were compared with normative data determined by Reitan (1955) which establishes values for neurologically normal and brain-damaged groups. Each patient's level of performance on specific tests was compared with these values determined by Reitan and thus categorized as "perfectly normal", "normal", "mildly impaired" or "seriously impaired". An overall measure of impairment was determined on the basis of the Halstead Impairment Index which was computed based on cut-off scores for the tests that were established by Halstead (1947). (2) A second method of inference was to look for the presence or absence of specific deficits (pathognomonic signs) that occur almost exclusively in persons with cerebral disorders and have lateralizing and localizing value. (3) The third

method of inference was to compare performances on the two sides of the body to assess the functional status of the two cerebral hemispheres. (4) Finally, the patterns and interrelationship of scores and specific deficits were evaluated as they relate to the various functions of different parts of the cerebral cortex. Tests used as part of this battery include the Category Test, Tactual Performance Test (TPT), Seashore Rhythm Test (SRT), Speech Sounds Perception Test (SSPT), Finger Tapping Test (FTT), Trail Making Test (TMT), Lateral Dominance Examination, Aphasia Screening Test. Tables 5 to 8 provide a list of test variables to be analysed from the HRNTB.

TABLE 5

Halstead-Reitan Neuropsychological Test Battery
Test Variables

1. Category Test - Error Score
2. TPT - Dominant Hand Time
3. TPT - Nondominant Hand Time
4. TPT - 2-Handed Time
5. TPT - Total Time
6. TPT - Number of Blocks Placed - Dominant Hand
7. TPT - Number of Blocks - Nondominant
8. Memory Score
9. Localization Score
10. SRT - # Correct
11. SSPT - Error Score
12. FTT - Dominant
13. FTT - Nondominant
14. Impairment Index
15. TMT A - Time/Errors
16. TMT B - Time/Errors
17. Grip Strength - Dominant
18. Grip Strength - Nondominant
19. Lateral Dominance - Right/Left

TABLE 6

Sensory Perceptual Examination
Test Variables

1. Tactile Imperceptions - Right Hand
2. Tactile Imperceptions - Left Hand
3. Tactile Imperceptions - Right Face
4. Tactile Imperceptions - Left Face
5. Auditory Imperceptions - Right Ear
6. Auditory Imperceptions - Left Ear
7. Visual Imperceptions - Right Ear
8. Visual Imperceptions - Left Eye
9. Tactile Suppressions - Right Hand
10. Tactile Suppressions - Left Hand
11. Tactile Suppressions - Right Face
12. Tactile Suppressions - Left Face
13. Auditory Suppressions - Right Ear
14. Auditory Suppressions - Left Ear
15. Visual Suppressions - Right Eye
16. Visual Suppressions - Left Eye
17. Finger Agnosia Suppressions - Right Hand
18. Finger Agnosia Suppressions - Left Hand
19. Finger Tip # Writing - Right Hand
20. Finger Tip # Writing - Left Hand

TABLE 7

Aphasia Screening Pathognomonic Indicators
Test Variables

1. Constructional Apraxia
2. Anomia
3. Verbal Apraxia
4. Dysgraphia
5. Dyslexia
6. Dysarthria
7. Acalculia
8. Reading Comprehension
9. Ideo-Kinetic Apraxia
10. Right-Left Disorientation
11. Auditory-Verbal Agnosia

The normative data used in these analyses were mean scores and standard deviations which have been established as values that distinguish normal from brain-damaged performances. Scores to be used for the various tests are presented in Table 8.

TABLE 8

Normative Means and Standard Deviations For the HRNTB

	Mean	S.D.
Category Test	33.97	17.20
TPT - Dominant	288.94	111.22
TPT - Nondominant	199.00	79.26
TPT - Both	118.07	57.75
Memory	8.30	1.33
Localization	5.70	2.24
Grip Strength-Dom.	44.20	13.01
Grip Strength-Ndom.	38.76	12.61
FTT-Dominant	48.38	7.76
FTT-NonDominant	44.54	6.76
SSPT (errors)	4.05	2.12
SRT (errors)	2.38	1.94
Finger Tip #-Writing-R	1.67	1.99
Finger Tip #-Writing-L	1.25	1.64
Trails B	52.05	15.36

(d) Patient History

A comprehensive patient history form was developed to include demographic information, personal

history of illness, accident, birth and developmental factors, education, family history of psychiatric illness, etc. Table 9 provides a list of variables to be analyzed from the patient history.

TABLE 9

Patient History
Test Variables

1. Duration of Illness
2. Educational Level
3. Marital Status
4. Medication

All psychological test measures used in the study were administered by a trained technician in accordance with standardized procedures.

E. Design and Data Analysis

The purpose of the study was to assess the homogeneous subgroupings of schizophrenics on the basis of patterns of clinical symptoms and neuropsychological functioning and to quantitatively and qualitatively assess

the interplay of these factors. Subgroupings of schizophrenics were, therefore, established as a basis from which to conduct further analysis. Data was analysed through the following means.

Initially, frequency distributions and measures of central tendency were determined for the entire study population for all variables to establish a basis from which to identify differences that might be present once the subjects were subgrouped. These measures of central tendency were compared with the normative means and standard deviations for the standardization populations of the various psychological tests used in the study.

(a) Establishment of Subgroups

Three separate means of subgrouping the schizophrenic population were then employed so that analysis of more homogeneous groups of schizophrenic subjects might be conducted.

Positive and Negative Symptom Subgroup. For the first subgrouping, two groups were established on the basis of Positive and Negative symptomatology using the rigorous diagnostic criteria established by Andreasen and Olsen

(1982). The means and standard deviations of a Positive Symptom Group and a Negative Symptom Group were compared and a statistical test of significance (Mann-Whitney U 2-tailed P) applied to determine whether or not statistically significant differences existed between the two groups.

Impairment Index Subgrouping. For the second subgrouping, subjects were categorized on the basis of HRNTB Impairment Index. Three subgroups were formed in the following manner.

Impairment Index Subgrouping

Group	Degree of Imprmt.	Index	Nbr. of Ss
1	unimpaired	0-.4	16
2	mild-moderate	.5-.7	18
3	mod.-severe	.8-1.0	19

This method of subgrouping addressed the need for homogeneity on the basis of degree of impaired neurological functioning. This method provided a viable quantitative means of subdividing members of the study population in order to allow homogeneity on the basis of degree of brain dysfunction.

Cluster Analysis Subgrouping. One other subgrouping of schizophrenic subjects was also determined. This subgrouping was established on the basis of a cluster analysis. Results from the neuropsychological data were subjected to a statistical cluster analysis. This was done to provide a more qualitative division of subjects into a homogeneous subgroup on the basis of similarity of neuropsychological functioning. On the basis of the cluster analysis of HRNTB data, the third subgrouping was established as follows.

Cluster Analysis Of HRNTB Subgrouping

Group	Nbr. of Ss
1	26
2	5
3	22

Following the establishment of subgroups, data were analysed through a variety of means to capture both qualitative and quantitative aspects inherent to the various subgroupings. Both the level of performance and pattern of performance between and within groups were analysed in the following manner.

(b) Analysis of Means and Standard Deviations

Means and standard deviations were computed for all subgroups and then compared to normative means from the standardization samples of the various psychological tests used in the study. Means were also, of course, compared across the various subgroups. Both the level and patterning of performance within and between groups were analysed as a way of descriptively discerning attributes inherent to each group as distinct from other groups and the normative population.

(c) Level of Performance Analysis

In addition to analysis of means and standard deviations, a comparison of the level of performance between the groups was analysed through conducting a multivariate analysis of variance (MANOVA). The MANOVA was used to determine whether or not there were significant differences between the groups with respect to level of performance on various test measures. Multivariate analysis of variances were computed for WAIS-R, HRNTB and clinical symptom variables in the following manner.

WAIS-R. The first set of analyses using MANOVA incorporated WAIS-R measures. Included in these analyses were the six Verbal Scale subtests (Information, Digit

Span, Vocabulary, Arithmetic, Comprehension, Similarities) and the Verbal I.Q. and the five Performance Scale subtests (Picture Completion, Picture Arrangement, Block Design, Object Assembly, and Digit Symbol) as well as the Performance I.Q.

Research Question. Are there statistically significantly different mean levels of performance between the study groups on the WAIS-R variables generally? Are there differences in level of functioning on Verbal, Performance, and Full Scale I.Q. values, brain sensitive subtests (Digit Symbol, Block Design, Digit Span, Arithmetic), and "hold" (Information, Vocabulary, Comprehension) measures?

HRNTB. The second set of analyses using MANOVA incorporated all HRNTB measures and supplementary neuropsychological test variables.

Research Question. Are there significantly different mean levels of performance among the three study groups on the HRNTB measures generally? Are there differences between groups with respect to: (1) level of performance on tests most sensitive to cerebral pathology; (2) level of performance on tests used to compute the

Impairment Index; (3) right-left differences which signify the functional status of the two hemispheres?

Clinical Symptoms. The third set of analyses using MANOVA incorporated clinical symptom measures. The analysis included all the positive symptom measures (hallucinations, delusions, bizarre behavior, formal thought disorder) and negative symptom measures (affective flattening, alogia, apathy, asociality, attention).

Research Question. Are there significantly different mean levels of performance between the three study groups in the level of symptoms present?

(d) Pattern Analysis

Following an assessment of whether or not the groups differed from one another on the various measures as determined through a MANOVA, an analysis of the profile patterning was conducted through an analysis of scattering of means and also through performing a discriminant analysis. In cases where the MANOVA results indicated significant group differences existed, a follow-up discriminant analysis procedure was used to determine on which variables the groups differed. Discriminant analysis

procedures were applied to all WAIS-R variables, HRNTB variables and Symptom variables for all the various subgroupings.

In the investigation of the subgrouped data, the following research questions were formulated.

Research Questions

1. Are there patterns which emerge signifying areas of intact functioning and areas of deficit compared to the normative population with respect to verbal functioning, perceptual organizational functioning, brain sensitive subtests, "hold" subtests, I.Q. values and overall performance?

2. What similarities and/or differences exist in the profile patterning of performances between the study groups?

3. Are there patterns which emerge signifying areas of intact functioning and/or areas of deficit compared to the normative population with respect to: (1) performance on tests most sensitive to cerebral pathology; (b) performance on tests used in determining the Impairment Index; (c) the comparative status of the two cerebral hemispheres; (d) all

HRNTB measures?

4. What similarities and/or differences reflecting areas of intact and/or deficit functioning exist in the patterning of performances between the three study groups?

5. Do the patterns of symptoms differ between the three study groups?

CHAPTER V

RESULTS AND DISCUSSION

A. Introduction

The total study population of schizophrenics included a sample of 53 subjects, 74% of whom were male and 26% female, with a mean age of 33 years and a median duration of illness of 66 months. Within this chapter, measures of central tendency for the entire population are presented first and comparisons are drawn between the performance of schizophrenic subjects and the normative means and standard deviations for the standardization population of the various psychological tests used in this study. Following a discussion of results of the entire study population, the sample was then subdivided and the subgroups were analysed both qualitatively and quantitatively through a combination of descriptive analysis of means and standard deviations as well as through a number of statistical procedures. The total sample of schizophrenics was subdivided for analysis on the basis of several criteria: (1) on the basis of rigorous diagnostic criteria for Positive and Negative symptom schizophrenia as outlined by Andreasen and Olsen (1982);

(2) on the basis of degree of cerebral impairment as determined by the Impairment Index of the HRNTB; (3) on the basis of a cluster analysis of neuropsychological test data; (4) on the basis of a cluster analysis of the symptom data.

An important caveat to the presentation and discussion of these results is the fact that the study population was relatively small due to rigorous inclusion criteria and availability of subjects. Statistical analyses of the subgrouped samples was necessarily limited and constrained by the fact of the small number of subjects and must be viewed circumspectly with this in mind.

B. Total Study Population Results

The total study population of schizophrenics consisted of 53 subjects. Measures of central tendency for the entire study population appear in Tables 10 and 11 and serve as a baseline from which further analyses of subgroupings of the study population may be considered. Following are results from both WAIS-R and HRNTB variables for the study population as a whole (N=53).

(a) WAIS-R Performance

The measures of central tendency for WAIS-R variables presented in Table 10 reveal that without exception, all I.Q. values and scaled scores obtained by the schizophrenic subjects for both Verbal and Performance Scales fell significantly below normative mean scores for the WAIS-R. Compared to standardized WAIS-R mean scores, the schizophrenic population demonstrated Low Average functioning for verbal comprehension and expression (V.I.Q. = 87.288; S.D. = 12.845) and visual perceptual organization (P.I.Q. = 84.442; S.D. = 10.493), with combined verbal and nonverbal abilities resulting in an overall Low Average Full Scale I.Q. (F.S.I.Q. = 84.846; S.D. = 10.554). All three I.Q. values fell within a narrow range reflecting a consistent level of verbal (left hemispheric) and nonverbal (right hemispheric) functioning.

Individual subtest scaled scores also fell uniformly within this Low Average range, with very little variability being apparent in the profile of individual subtests. An exception to this is evident in performance of the Digit Symbol subtest which was slightly lower, falling in the Borderline range. This subtest is considered to be one of the most sensitive indicators of brain dysfunction on the WAIS-R. Generally, compared to normals, the schizophrenic population as a whole were

characterized by a Low Average level of intellect.

Table 10

**Measures of Central Tendency - WAIS-R Variables
Total Study Population (N=53)
Compared to Normative Population Test Means**

	Study Population Mean	S.D.	Normative Mean	S.D.
V.I.Q.	87.29	12.85	100	10
P.I.Q.	84.44	10.48	100	10
F.S.I.Q.	84.85	10.55	100	10
Info	7.87	2.98	10	3
DS	7.75	2.38	10	3
Vocab	7.94	2.97	10	3
Arith	7.69	2.76	10	3
Comp	7.08	3.16	10	3
Sim	7.52	3.34	10	3
PC	7.60	2.80	10	3
PA	7.17	2.69	10	3
BD	8.23	2.57	10	3
OA	7.65	2.82	10	3
DSy	5.56	2.09	10	3

(b) HRNTB Performance

A similar trend was evident in the schizophrenics'

performance on the brain-sensitive measures of the HRNTB. In Table 11, means and standard deviations on the HRNTB variables for the study population as a whole are presented, along with normative means for these test measures. Without exception, the schizophrenic population performed more poorly on all measures of this battery compared to the normative population and thus reveal a poorer level of adaptive brain functioning generally.

(c) Summary of Total Population Results

Compared to the standardization sample for both the WAIS-R and HRNTB tests, the schizophrenic study population as a whole demonstrated Low Average intellect, but with fairly equally developed Verbal, Performance and Full Scale I.Q.'s, and consistency between individual subtests as well, with the exception of Borderline functioning on the Digit Symbol subtest. Poor adaptive functioning on the HRNTB was also evident and the profile for the schizophrenic group as a whole is one of generally inefficient cognitive functioning.

C. Positive and Negative Symptom Subgrouping Analyses

Based on established diagnostic criteria for

TABLE 11

Measures of Central Tendency - HRNTB Variables
Total Study Population (N=53)
Compared to Normative Population Test Means

	Study Population		Normative	
	Mean	S.D.	Mean	S.D.
Cat	70.93	32.60	33.97	17.20
TPTDom	516.67	201.53	288.94	111.22
TPTNDom	431.29	207.62	199.00	79.26
TPTBoth	308.29	219.49	118.07	57.75
TPTTot	1236.16	572.39	----	----
Memory	6.62	1.66	8.30	1.33
Local	2.09	2.01	5.70	2.24
SRT	7.39	4.37	2.38	1.94
SSPT	8.85	6.02	4.05	2.12
FTTDom	42.65	8.95	48.38	7.76
FTTNDom	39.22	8.23	44.54	6.76
TrailsA	57.02	40.80	----	----
TrailsB	135.15	84.22	52.05	15.36
GripDom	37.02	12.23	44.20	13.01
GripNDom	34.92	10.83	38.76	12.61

positive and negative symptom schizophrenics (Andreasen and Olsen, 1982), determined on the basis results from the SANS/SAPS symptom checklists, a group of Positive Symptom schizophrenics (N=7) and a group of Negative Symptom (N=7) schizophrenics were formed. There were 31 out of 53 SANS/SAPS checklists completed by hospital staff members who were sufficiently familiar with the schizophrenic subject to be able to complete the Likert Scale symptom checklist. For the remaining 22 subjects, symptom checklists were completed from chart information, as described previously and were not included in this analysis as symptoms were rated on a "present/absent" basis rather than rated for severity on the Likert Scale. It is interesting to note that of the 31 SANS/SAPS symptom checklists completed by staff, only 14 subjects (45%) could be categorized according to either positive or negative diagnostic criteria. Diagnostic categorization of either positive or negative symptom schizophrenics, as determined by the SANS/SAPS, essentially indicate an illness that is predominantly characterized by either positive symptoms (hallucinations, delusions, bizarre behavior and/or formal thought disorder) without the presence of negative symptoms, or, alternatively, predominantly negative symptoms (affective blunting, alogia, apathy, asociality and/or attention deficit) without the presence of positive

symptoms. A total of 14 subjects could be classified in accordance with these more purely defined symptom patterns. The remaining 17 subjects (55%) were characterized by a mixture of both positive and negative symptoms forming their clinical picture.

An analysis of these 14 subjects was conducted. Tables 12 and 13 respectively contain the means and standard deviations for all WAIS-R and HRNTB variables for the Positive Symptom group and the Negative Symptom group. As an adjunct, a nonparametric test of significance (Mann-Whitney U 2-tailed P) was used to determine whether or not statistically significant differences existed between the two groups on any of the variables.

(a) Research Questions and Hypotheses

In the investigation of the Positive and Negative Symptom Subgroups, the following research questions and hypotheses were formulated:

Research Question 1: Are there differences in the mean level and patterning of performance between the Positive and Negative Symptom study groups with respect to Verbal, Performance and Full Scale I.Q. values?

Reseach Question 2: Are there differences in the mean levels and patterning of performance between the Positive and Negative Symptom study groups with respect to individual subtest performance?

Research Question 3: Are there differences in the mean levels and patterning of performance between the Positive and Negative Symptom study groups on HRNTB variables?

Hypothesis 1: There is no difference in Positive and Negative Symptom schizophrenics on WAIS-R I.Q. and individual subtest variables.

Hypothesis 2: There is no difference in Positive and Negative Symptom schizophrenics on HRNTB variables.

Hypothesis 3: There is no difference in Positive and Negative Symptom schizophrenics with respect to daily dosage of neuroleptic medication being administered.

Hypothesis 4: There is no difference in Positive and Negative Symptom schizophrenics with respect to the duration of their illness.

(b) WAIS-R Performance

The Positive Symptom group was characterized by more normal intellectual functioning (see Table 12), obtaining Verbal (V.I.Q. = 92.857; S.D. = 17.620), Performance (P.I.Q. = 90.143; S.D. = 9.940) and Full Scale I.Q. values (F.S.I.Q. = 91.000; S.D. = 14.434) that fall within the Average range, although just barely (Average WAIS-R I.Q. range = 90 to 110). For the most part, I.Q. values and individual subtest scaled scores tended to fall within a narrow range suggesting a reasonably even development of intellectual skills within the lower end of the Average range. One exception to this was evident as revealed by Borderline functioning on the Digit Symbol subtest.

The Negative Symptom group was characterized by a similar patterning of WAIS-R scores to the Positive Symptom group; however, their performance typically was lower reflecting a general pattern of more poorly demonstrated intellectual functioning. Verbal (V.I.Q. = 85.000; S.D. = 13.379), Performance (P.I.Q. = 82.143; S.D. = 9.477) and Full Scale I.Q. values (F.S.I.Q. = 82.286; S.D. = 7.135) all fell consistently within the Low Average range of mental ability. Generally, the Negative Symptom group

TABLE 12

POSITIVE AND NEGATIVE SYMPTOM SUBGROUPING
Measures of Central Tendency
Mann-Whitney U 2-Tailed P
WAIS-R Variables

Variable	Positive (N=7) Mean	S.D.	Negative (N=7) Mean	S.D.	2-Tailed P
V.I.Q.	92.86	17.62	85.00	13.38	0.41
P.I.Q.	90.14	9.94	82.14	9.48	0.11
F.S.I.Q.	91.00	14.44	82.29	7.14	0.25
Info	8.86	3.44	7.00	2.52	0.33
D.S.	8.29	1.80	8.57	2.94	0.51
Vocab.	10.00	3.42	6.143	3.53	0.03*
Arith	8.29	3.40	7.71	2.56	0.79
Comp	7.86	3.98	5.71	3.20	0.20
Sim	8.86	3.93	6.44	1.71	0.09
PC	8.57	2.50	7.43	3.10	0.40
PA	8.71	3.68	6.71	1.11	0.33
BD	9.43	1.40	7.57	2.57	0.12
OA	9.86	1.07	7.43	3.74	0.07
DSy	5.29	.95	6.29	3.04	0.51

Mann-Whitney U - 2-Tailed P
Duration of Illness by Positive and Negative Group: P = 0.7981

Daily Dosage of Neuroleptic Medication by Group: P = 0.5653

scored approximately 8 points lower on I.Q. scores compared to the Positive Symptom group.

Individual subtest scaled scores for the Negative group were characterized by several subtest scores that actually fell within the Borderline range. Notably, these included three subtests from the Verbal scale (Vocabulary, Comprehension and Similarities) and the Digit Symbol Subtest from the Performance scale. In effect, the Negative Symptom group appeared to perform slightly more poorly than the Positive Symptom group generally, with specific left-hemispheric, verbal comprehension and expression abilities being particularly weak.

A statistical test of significance (Mann-Whitney U - 2-Tailed P) was applied to determine whether or not the differences between these two groups reach statistical significance. One variable, namely, the Vocabulary subtest, proved to be statistically significantly different between the groups (2-Tailed P = 0.0342). It is notable in Table 12 that despite the attempt to rigorously establish homogeneous subgroupings of schizophrenic patients, there is still a wide dispersion on some test scores as is evident in the standard deviations. Both the Positive and Negative group are characterized by wide dispersion of

scores on some variables. This wide dispersion present in some of the test scores for both groups reveals the complex nature of schizophrenia. The null hypothesis stated earlier in this section as hypothesis 1 may thus be rejected.

(c) HRNTB Performance

Within the brain-sensitive measures of the HRNTB, the Negative symptom group's performance was equivalent to the Positive symptom group's performance on some variables but worse on others. Generally, consistent with their intellectual functioning, the Positive Symptom group demonstrated a lesser degree impairment of adaptive functions on the HRNTB compared to the Negative Symptom Group, with a pattern of performance that may be described generally as less efficient when compared to normals.

In contrast, the Negative Symptom group performed more poorly than the Positive Symptom group on a number of tests. Gross motor grip strength was performed more poorly by the Negative Symptom group (GripDom Mean = 34.788; GripNDom = 29.84) than the Positive group (GripDom Mean = 46.000; GripNdom = 42.143), as were Category test (Negative group mean error rate = 67.137; Positive group mean error

TABLE 13

POSITIVE AND NEGATIVE SYMPTOM SUBGROUPING
Measures of Central Tendency
Mann-Whitney U 2-Tailed P
HRNTB Variables

	Positive		Negative		
	Mean	S.D.	Mean	S.D.	2-Tailed P
Cat	51.71	29.58	67.13	25.71	0.37
TPTDom	447.57	144.27	423.62	152.82	0.85
TPTNDom	397.57	160.41	407.94	175.71	0.75
TPTBoth	275.14	179.88	271.00	166.32	0.85
Memory	6.86	1.86	6.18	1.33	0.44
Local	1.71	2.56	1.60	1.28	0.6
SRT	4.86	3.67	9.57	6.75	0.90
SSPT	4.46	.65	4.38	.77	0.16
FTTDom	44.57	6.48	43.67	7.73	0.80
FTTNDom	41.86	4.74	40.92	2.87	0.95
Imprmt	6.00	4.00	6.35	1.25	0.85
TrailB	113.29	59.33	118.86	68.59	0.95
GripDom	46.00	16.66	34.79	12.15	0.16
GripNDom	42.14	14.92	29.85	11.12	0.096
DDNeurol**	569.29	400.34	583.86	655.65	0.57

(Chlorpromazine equivalent in mg. units)**

rate = 51.705), and SRT performances (Negative group mean error rate = 9.571; Positive group mean error rate = 4.857). The pattern of impaired adaptive functioning of the Negative Symptom group is suggestive of bilateral fronto-temporal impairment. Taking into account WAIS-R results previously discussed, the Negative Symptom group, compared to the Positive Symptom group appeared to be characteristically more cognitively impaired with language and gross motor functioning being most strikingly affected, implicating bilateral frontal involvement with greater compromise being evident in the dominant hemisphere.

A statistical test of significance (Mann-Whitney U - 2-Tailed P) was applied to determine whether or not differences between these two groups reach statistical significance. Although none of the differences were statistically significant, the Grip Strength variables came closest to reaching significance (GripDom 2-Tailed P = 0.1594; GripNDom 2-Tailed P = 0.0963). In this instance, the null hypothesis stated as hypothesis 2 earlier in this section may be accepted in that no statistically significant differences exist between these two study groups on the HRNTB variables..

Two factors contributing to the inconsistency of

findings in research with schizophrenics appear in the literature, namely chronicity and effects of medication. For this reason, these factors were assessed to determine whether or not significant differences between subgroups exist. The mean ranked daily dosage of neuroleptic medication (P = 0.7981) received by each group as well as the mean ranked duration of illness (P = 0.5653) (as determined from the point of their first psychiatric contact to the point of the psychological assessment conducted as part of this study) were analysed between groups and found to be nonsignificant. Thus, the null hypothesis stated as hypotheses 3 and 4 may be accepted.

(d) Summary of Positive and Negative Subgrouping Results

In summary, Positive (N=7) and Negative (N=7) symptom groups were formed on the basis of diagnostic criteria from the SANS/SAPS. Descriptive analysis of mean scores for WAIS-R and HRNTB variables revealed that the Positive Symptom Group generally functioned within the lower end of the Average range intellectually, while the Negative Symptom Group demonstrated Low Average intellectual functioning, averaging approximately 8 I.Q. points lower than the Positive Symptom Group on the whole. Both groups, however, functioned in the Borderline range on

the Digit Symbol subtest which is considered quite sensitive to cerebral dysfunction generally. More scattering of scores was evident for the Negative Symptom Group with the Vocabulary, Comprehension and Similarities subtests on the Verbal Scale being most poorly performed implying impairment of left hemispheric verbal comprehension and expression. Only the Vocabulary subtest, however, reached a statistically significant level (2 - Tailed P = 0.0342). Descriptive mean score comparisons of HRNTB variables revealed a trend for the Negative Symptom Group to perform more poorly than the Positive Symptom Group for gross motor grip strength for both dominant and nondominant hands (bilateral frontal), the Category Test (left, and/or bilateral prefrontal) reflecting general thinking ability in which logical analysis, cognitive flexibility and abstract concept formation are required in order to efficiently problem-solve and SRT (temporal) requiring complex attention and concentration as well as auditory discrimination of different patterns of rhythms. In essence, it may be stated that the Positive Symptom group was characteristically inefficient in their cognitive functioning as compared to normals but that no specific identifying deficit pattern emerged as apart from this generalized inefficiency. In contrast, the Negative Symptom Group revealed a deficit pattern characterized by

bilateral fronto-temporal impairment with greater compromise of the dominant hemisphere being evident.

D. Impairment Index Subgrouping Analyses

Given the fact that so few schizophrenic subjects could be diagnostically categorized according to the positive and negative symptom syndrome model and stringent diagnostic criteria, further subgrouping methods were used in order to derive more homogeneous subgroupings of the schizophrenic population for analysis.

Two additional subgroupings were established: (1) Impairment Index Subgrouping and, (2) Cluster Analysis Subgrouping of the HRNTB data.

The Impairment Index of the HRNTB is a ratio of number of impaired performances on the battery. It serves primarily as a reliability index, but also may be used to some extent as a measure of severity of cerebral impairment. Tests included in determining the Impairment Index are: (1) Category Test; (2) Tactual Performance Test, Total Time; (3) TPT Memory; (4) TPT Location; (5) SSPT; (6) SRT; (7) Finger Tapping Test (Halstead, 1947). Three subgroups were formed using this Index. Group 1 was

established as an "unimpaired" group with Impairment Indexes ranging from 0.0 to .4 (N=16); Group 2 a "mildly to moderately" impaired group with Impairment Indexes ranging from .5 to .7 (N=18); and Group 3 a "severely" impaired group with Impairment Indexes ranging from .8 to 1.0 (N=19).

Tables 14, 17 and 20 present the means and standard deviations for the study groups on each of the variables of the WAIS-R, HRNTB and SANS/SAPS. Two further analyses were computed with all three sets of variables. A multivariate analysis of variance (MANOVA) was followed-up with a discriminant analysis; however, it should be reiterated that these results should be viewed cautiously keeping in mind the small sample size to which these statistics are applied.

(a) Research Questions and Hypotheses

In the investigation of Impairment Index subgroupings, the following research questions and hypotheses were formulated:

Research Question 1: Are there differences in the mean level and patterning of performance between the three

Impairment Index study groups with respect to Verbal, Performance and Full Scale I.Q. values?

Research Question 2: Are there differences in the mean levels and patterning of performance between the three Impairment Index study groups with respect to individual subtest performance?

Research Question 3: Are there differences in the means levels and the patterning of performance between the three Impairment Index study group in their functioning on HRNTB tests?

Research Question 4: Do the symptom patterns differ between the three Impairment Index study groups?

Hypothesis 1: There is no difference in performance on WAIS-R I.Q. and individual subtest variables between the three groups established on the basis of the Impairment Index criteria.

Hypothesis 2: There is no difference in performance on HRNTB variables between the three study groups established on the basis of Impairment Index criteria.

Hypothesis 3: There is no difference in the degree of various symptoms present between the three study groups established on the basis of Impairment Index criteria.

Hypothesis 4: There is no difference between the three study groups established on the basis of Impairment Index criteria with respect to daily dosage of neuroleptic medication being administered.

Hypothesis 5: There is no difference between the three study groups established on the basis of Impairment Index criteria with respect to the duration of their illness.

(b) WAIS-R Performance

The multivariate analysis of variance (MANOVA) of WAIS-R variables presented in Table 14 was found to be nonsignificant ($F = 1.576$, $df = 28/74$, $P = 0.06233$) by the Wilks' Lambda Criterion, although approaching a level of statistical significance. Examination of the mean scores between groups indicated a general trend that Group 1, the "unimpaired" group performed better across all WAIS-R variables, with Verbal (V.I.Q. = 97.200; S.D. = 14.098),

Performance (P.I.Q. = 94.133; S.D. = 9.070) and Full Scale I.Q.'s (F.S.I.Q. = 94.800; S.D. = 10.551) falling consistently and evenly within the Average range of mental ability. Individual subtest scaled scores similarly reflected very little scatter and thus suggest an even development of intellectual skills, with the Digit Symbol subtest falling only slightly lower in the Low Average range.

Groups 2, the "mild to moderate" and 3, the "severely" impaired group tended to be similar to each other with respect to level and pattern of intellectual functioning. Both groups obtained Verbal (Group 2 V.I.Q. = 84.000; Group 3 V.I.Q. = 82.579), Performance (Group 2 P.I.Q. = 80.444; Group 3 P.I.Q. = 80.579) and Full Scale I.Q. (Group 2 F.S.I.Q. = 81.278; Group 3 F.S.I.Q. = 80.368) values that fall at the low end of the Low Average range of intellectual ability, with individual subtest scaled scores ranging reasonably narrowly from Borderline to Low Average. Group 1 was distinguishable from Groups 2 and 3 on the basis of overall level of functioning, with group 1 more closely representing an Average level of intellect. On average, Group 1 performed approximately 13 I.Q. higher than both Groups 2 and 3 on all three I.Q. values.

TABLE 14

MANOVA

IMPAIRMENT INDEX SUBGROUPING
Measures of Central Tendency
Multivariate Analysis of Variance (MANOVA)
WAIS-R Variables

(Group 1 - Unimpaired - Index - 0 - .4; Group 2 - Mild-Moderate - Index = .5 - .7; Group 3 - Severe - Index = .8 - 1)

	1 (N=16)		2 (N=18)		3 (N=19)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
V.I.Q.	97.20	14.10	84.00	11.45	82.58	8.54
P.I.Q.	94.13	9.07	80.44	8.15	80.58	8.64
F.S.I.Q.	94.80	10.55	81.28	8.14	80.37	7.07
Info	9.67	2.69	7.22	3.35	7.05	2.27
DS	9.07	2.28	8.00	2.22	6.47	2.04
Vocab	9.67	2.87	7.22	3.14	7.26	2.48
Arith	10.20	2.81	6.67	2.20	6.68	1.89
Comp	8.93	3.81	6.61	3.07	6.05	1.99
Sim	9.47	3.34	7.29	3.16	6.21	2.57
PC	9.73	1.98	7.33	2.95	6.16	2.18
PA	9.33	2.82	6.83	2.23	5.79	1.98
BD	10.20	1.82	7.56	2.04	7.32	2.77
OA	9.20	2.34	6.83	2.26	7.21	3.26
DSy	7.00	2.10	5.48	1.87	4.68	1.73

Manova Probability = 0.06233

Kruskal-Wallis 1-Way Anova
Daily Dosage of Neuroleptic Medication by Subgroup: P = 0.1828

Mann-Whitney U - 2-Tailed P
Duration of Illness by Subgroup: 2-Tailed P = 0.3051

Since the level of significance from the multivariate analysis of the WAIS-R variables approached significance, a follow-up discriminant analysis procedure was used to determine on which variables the groups may differ. Data from this analysis are shown in Tables 15 and 16. The canonical discriminant functions revealed in Table 15 indicated that significant discrimination (Chi-Square = 43.796, df = 28, P = 0.0291) was achieved on the first function, but not on the second (Chi-Square = 11.411, df = 13, P = 0.5765). Standardized canonical discriminant function coefficients listed in Table 16 under function 1 show three large contributors: Full Scale I.Q., Performance I.Q., and Verbal I.Q. This converges with the previously discussed observation regarding the average 13 point discrepancy between the mean I.Q. values between Group 1 compared to Groups 2 and 3. The percent of "grouped" cases correctly classified on the basis of this discriminant function analysis were 69.23%. Members in Groups 1 and 3 were most accurately classified, with correct classification results being 73.3% and 73.7% respectively, while members in Group 2 were classified less accurately at 61.1%.

(c) HRNTB Performance

Although results from the multivariate analysis

TABLE 15

Discriminant Analysis

SUBGROUPING ACCORDING TO IMPAIRMENT INDEX
WAIS-R Variables

	Wilks' Lambda	Univariate F	Significance
V.I.Q.	0.75	8.09	0.0009
P.I.Q.	0.65	13.38	0.0000
F.S.I.Q.	0.63	14.33	0.0000
Info	0.85	4.37	0.0180
DS	0.88	6.14	0.0042
Vocab	0.86	3.98	0.0251
Arith	0.66	12.66	0.0000
Comp	0.85	4.26	0.0196
Sim	0.83	4.99	0.0107
PC	0.72	9.17	0.0004
PA	0.71	10.18	0.0002
BD	0.75	7.90	0.0011
OA	0.87	3.57	0.0354
Dsy	0.79	6.57	0.0030

Canonical Discriminant Functions

Function	Wilks' Lambda	Chi-Square	D.F.	Significance
1	0.3568264	43.796	28	0.0291
2	0.7645359	11.411	13	0.5765

TABLE 16

IMPAIRMENT INDEX SUBGROUPING - WAIS-R Variables
Standardized Canonical Discriminant Function Coefficients

	Func 1	Func 2
V.I.Q.	-1.44	-0.46
P.I.Q.	-1.48	-0.46
F.S.I.Q.	2.91	-0.13
Info	-0.35	0.88
DS	-0.13	0.82
Vocab	-0.15	-0.92
Arith	0.48	-0.74
Comp	0.47	0.10
Sim	-0.43	0.70
PC	0.47	0.15
PA	0.01	0.54
BD	0.33	0.15
OA	-0.03	-0.26
DSy	0.52	0.11

Classification Results

		Predicted Group Membership		
Actual Group	**N**	**1**	**2**	**3**
1	15	11 73.3%	3 20.0%	1 6.7%
2	18	3 16.7%	11 61.1%	4 22.2%
3	19	1 5.3%	4 21.1%	14 73.7%

Percent of "Grouped" cases correctly classified: 69.23%

of variance conducted on WAIS-R variables did not quite reach statistical significance, the multivariate analysis of variance conducted with HRNTB variables presented in Table 17 was found to be significant ($F = 7.1969$, $df = 38/64$, $P = 0.0$) and so the null hypothesis stated as hypothesis 2 earlier in this section may be rejected and it may be said that the three groups differed significantly on these variables.

Not surprisingly, an examination of the mean scores for the HRNTB variables reflected a pattern of greater impairment on virtually all variables across the groups from Group 1 - "unimpaired" to Group 3 - "severely" impaired. For example, the mean error rate for Group 1 on the Category Test (Mean = 53.286) tended to be on the borderline between unimpaired and impaired; Group 2 was slightly more impaired on the Category Test (Mean = 66.400); and Group 3 the most severely impaired (Mean = 89.471). The difference between these three groups appeared to be more related to level of performance with deteriorating performances being apparent across groups, but the pattern of performance does not appear to differ in any outstanding way.

The multivariate analysis of variance of the

TABLE 17

MANOVA - 1

IMPAIRMENT INDEX SUBGROUPING
Measures of Central Tendency
Multivariate Analysis of Variance (MANOVA)
HRNTB Variables

		1 (N=16)		2 (N=18)		3 (N=19)	
		Mean	S.D.	Mean	S.D.	Mean	S.D.
a.	Cat	53.29	34.46	66.40	29.76	89.47	24.33
b.	TPTDom	365.71	126.41	542.47	208.39	636.29	165.99
c.	TPTNDom	324.31	132.71	468.33	236.67	486.16	134.11
d.	TPTBoth	178.14	98.26	349.47	248.95	396.43	214.44
e.	TPTTotal	844.93	285.02	1369.12	663.72	1467.14	498.31
f.	Memory	7.79	.975	6.71	1.40	5.36	1.66
g.	Local	3.87	2.56	1.71	1.80	1.57	1.28
h.	SRT(error)	5.73	3.22	6.80	4.89	10.00	4.35
i.	SSPT(error)	6.25	5.29	8.30	7.32	11.53	4.34
j.	FTTDom	48.56	5.49	39.24	11.04	40.74	6.89
k.	FTTNdom	45.19	6.29	34.56	9.89	38.11	5.86
l.	Imprmt	.38*	.14	.63*	.07	.93*	.08
m.	TrailB	79.69	19.89	130.94	74.89	185.84	97.69
n.	GripDom	40.71	13.52	35.86	11.51	34.88	11.60
o.	GripNDom	38.49	11.86	32.13	10.14	34.25	10.20

Manova Probability = 0.0*

TABLE 18

IMPAIRMENT INDEX SUBGROUPING - HRNTB Variables

	Wilks' Lambda	Univariate F	Significance
Cat	0.86	3.98	0.03
TPTDom	0.28	63.92	0.0
TPTNDom	0.38	40.26	0.0
TPTBoth	0.26	71.38	0.0
TPTTot	0.13	173.9	0.0
Memory	0.84	4.75	0.01
Local	0.83	5.09	0.01
SRT	1.00	0.70	0.93
SSPT	0.97	0.89	0.42
FTTDom	0.74	8.85	0.0001
FTTNDom	0.72	9.55	0.0003
TrailB	0.79	6.45	0.0032
GripDom	0.93	1.93	0.16
GripNDom	0.98	0.64	0.53

Canonical Discriminant Functions

Function	Wilks' Lambda	Chi-Square	D.F.	Significance
1	0.0587227	130.41	18	0.0000
2	0.6996143	16.432	8	0.0366

TABLE 19

IMPAIRMENT INDEX SUBGROUPING - HRNTB Variables
Standardized Canonical Discriminant Function Coefficients

	Func 1	Func 2
Cat	-0.21	-0.31
TPTDom	0.35	0.15
TPTBoth	0.17	-0.75
TPTTot	0.90	0.35
Local	-0.08	-0.49
SSPT	0.31	0.08
FTTDom	-0.86	-0.91
FTTNDom	0.45	1.44
TrailB	-0.32	0.81

Classification Result

		Predicted Group Membership		
Actual Group	N	1	2	3
1	26	26 100.0%	0 0.0%	0 0.0%
2	5	0 0.0%	5 100.0%	0 0.0%
3	22	1 4.5%	0 0.0%	21 95.5%

Percent of "Grouped" cases correctly classified: 98.11%

HRNTB variables was followed-up by a discriminant analysis procedure to determine where the differences between groups occur most prominantly. Data from this analysis are shown in Tables 18 and 19. The canonical discriminant functions revealed in Table 18 indicated that significant discrimination (Chi-Square = 130.41, df = 18, P = 0.0000) was achieved on the first function and on the second function (Chi-Square = 16.432, df = 8, P = 0.0366). Standardized canonical discriminant function coefficients listed in Table 19 under function 1 show that TPTTot, FTTDom, FTTNDom and TPTDom rank as the four variables entered into the analysis first, thus having the greatest discriminating power. It is noteworthy that all of these variables measure motor functions of the frontal lobes with both right and left hemispheres being implicated. The percent of "grouped" cases correctly classified by this discriminant analysis is 98.11%, with 100% of Groups 1 and 2 being correctly classified and 95.5% of Group 3 being correctly classified.

(d) Symptom Data

The multivariate analysis of variance of the symptom variables presented in Table 20 was found to be significant (F = 2.5316, df = 22/80, P = 0.00138)

TABLE 20

MANOVA - 2

IMPAIRMENT INDEX SUBGROUPING
Measures of Central Tendency
Multivariate Analysis of Variance (MANOVA)
Symptom Variables

	1 (N=16)		2 (N=18)		3 (N=19)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Halluc	1.38	1.20	1.72	1.64	1.42	1.47
Delus	3.63	2.42	2.61	2.79	2.73	2.08
BizarreBeh	.75	.78	.94	1.00	.95	.91
ThghtDis	1.31	1.66	2.06	2.49	2.26	1.76
AffBlunt	1.06	1.65	1.78	1.56	.95	.97
Alogia	.50	1.10	1.83	1.34	.84	1.19
Apathy	1.06	1.12	1.39	1.09	.84	1.02
Asocial	1.00	1.41	1.94	1.73	1.21	1.51
Attent	.50	.73	.67	.84	.47	.84
Positive	7.00	---	7.00	---	7.00	---
Negative	4.00	---	8.00	---	4.00	---

Manova Probability = 0.00138*

suggesting that differences between the groups existed with respect to symptoms. An examination of the mean scores between groups indicated that Group 2 differed by virtue of seeming to be characterized by a greater preponderance of negative symptomatology in comparison to Groups 1 and 3, although these differences are slight.

The significant multivariate analysis of variance of the symptom variables was followed-up by a discriminant analysis procedure to determine where the differences between groups occurred. Data from this analysis are shown in Tables 21 and 22. The canonical discriminant functions revealed in Table 21 were found to be nonsignificant on the first function (Chi-Square = 23.331, df = 18, P = 0.1782) and, of course, the second function (Chi-Square = 5.4016; df = 8, 0.7139). Classification results of this discriminant analysis produced only a 58.49% correct classification of "grouped" cases, as shown in Table 22. In effect, it appears that the symptoms of this analysis were not good predictors of level of brain impairment, since the three groups were established on this basis.

Again, the two factors contributing to the inconsistency of findings in research with schizophrenics,

Table 21
IMPAIRMENT INDEX SUBGROUPING - Symptom Variables

	Wilks' Lambda	Univariate F	Significance
Halluc	0.99	0.30	0.75
Delus	0.97	0.86	0.43
Bizarre Beh	0.99	0.22	0.77
ThghtDis	0.96	1.05	0.36
AffBlunt	0.93	1.85	0.17
Alogia	0.81	5.87	0.01
Apathy	0.95	1.21	0.31
Asocial	0.93	1.76	0.183
Attent	0.99	0.30	0.74

Canonical Discriminant Functions

Function	Wilks' Lambda	Chi-Square	D.F.	Significance
1	0.6021869	23.331	18	0.1782
2	0.8892861	5.4016	8	0.7139

Table 22

IMPAIRMENT INDEX SUBGROUPING - Symptom Variables
Standardized Canonical Discriminant Function Coefficients

	Func 1	Func 2
Halluc	0.73	-0.31
Delus	-0.86	0.66
BizarreBeh	0.38	-0.25
Thgtdis	0.02	-0.79
Affblunt	0.06	0.22
Alogia	0.74	0.35
Apathy	-0.37	0.58
Asocial	0.65	-0.13
Attent	-0.44	0.23

Classification Results

		Predicted Group Membership		
Actual Group	N	1	2	3
1	16	9 56.3%	1 6.3%	6 37.5%
2	18	3 16.7%	11 61.1%	4 22.2%
3	19	3 15.8%	5 26.3%	11 57.9%

Percent of "Grouped" cases correctly classified: 58.49%

namely chronicity and effects of medication, were assessed to determine whether or not significant differences between subgroups existed. The mean ranked daily dosage of neuroleptic medication (P = 0.1828) received by each group as well as the mean ranked duration of illness (P = 0.3051) were analysed between groups and both found to be nonsignificant. Thus the null hypotheses stated as hypotheses 4 and 5 earlier in this section may be accepted.

(e) Summary of Impairment Index Subgrouping Results

In summary, three subgroupings were established on the basis of Impairment Index criteria such that Group 1 (N = 16) was characterized as an "unimpaired" group (I.I. = 0.0 to .4), Group 2 (N = 18) a "mild to moderate" group (I.I. = .5 to .7) and Group 3 (N = 19) a "severely" impaired group. Descriptive analysis of mean scores for WAIS-R and HRNTB variables revealed that Group 1, the "unimpaired" group, performed better intellectually than both Groups 2 and 3, averaging approximately 13 I.Q. points better across all three I.Q. values and demonstrating an Average level of intellect. Groups 2 ("mild to moderate") and 3 ("Severe") appeared similar to each other with respect to intellectual functioning, both

with all three I.Q. values falling at the lower end of the Low Average range. More distinction between all three groups was evident on the analysis of means for the HRNTB variables. However, the distinction between groups appeared to be related to level of performance, with deteriorating performances being apparent across groups. The pattern of performance did not appear to differ in any outstanding way. An analysis of mean scores for the symptom data revealed a trend in that Group 1 appeared the least symptomatic, Group 2 appeared to be characterized by an equal distribution of both positive and negative symptoms and was distinguishable from both Groups 1 and 3 by virtue of having more negative symptoms.

E. Cluster Analysis of HRNTB Data Subgrouping Analysis

In continuing to follow the idea that heterogeneous groups of schizophrenics may be subdivided into more homogeneous subgroups for analysis, a cluster analysis of the HRNTB data was performed in order to derive more naturally occurring homogeneous subgroups inherent to this population. This cluster analysis of HRNTB data resulted in the derivation of 3 subgroupings of the 53 subjects, with Group 1 being comprised of 26 subjects, Group 2 only 5 subjects and Group 3 comprising

22 subjects.

The same method of analysis was used for this subgrouping of the schizophrenic population as was used for the Impairment Index subgroupings. These data are presented in Tables 23 through 31. Tables 23, 26 and 29 present the means and standard deviations for the study groups on each of the variables of the WAIS-R, HRNTB and SANS/SAPS. Two further analyses were computed with all three sets of variables as well. A multivariate analysis of variance was followed-up with a discriminant analysis. Results from discriminant analyses appear in Tables 24 and 25 for WAIS-R variables, Tables 27 and 28 for HRNTB variables and Tables 30 and 31 for symptom variables.

(a) Research Questions and Hypotheses

In the investigation of the Cluster Analysis of the HRNTB data subgrouping, the following research questions and hypotheses were formulated:

Research Question 1: Are there differences in the mean level and patterning of performance between the three Cluster Analysis of HRNTB data study groups with respect to Verbal, Performance and Full scale I.Q. values?

Research Question 2: Are there differences in the mean levels and patterning of performance between the three Cluster Analysis of HRNTB data study groups with respect to individual subtest performance on the WAIS-R?

Research Question 3: Are there differences in the mean levels and patterning of performance between the three Cluster Analysis of HRNTB data study groups with respect to their functioning on HRNTB tests?

Research Question 4: Do symptom patterns differ between the three study groups?

Hypothesis 1: There is no difference in performance on WAIS-R I.Q. and individual subtest variables between the three groups established on the basis of the Cluster Analysis of the HRNTB data.

Hypothesis 2: There is no difference in performance on HRNTB variables between the three study groups established on the basis of the Cluster Analysis of HRNTB data.

Hypothesis 3: There is no difference in the degree of various symptoms present between the three study

groups established on the basis of the Cluster Analysis of the HRNTB.

Hypothesis 4: There is no difference between the three study groups established on the basis of the Cluster Analysis of the HRNTB data with respect to daily dosage of neuroleptic medication being administered.

Hypothesis 5: There is no difference between the three study groups established on the basis of the Cluster Analysis of the HRNTB data with respect to the duration of their illness.

(b) WAIS-R Performance

The multivariate analysis of variance of WAIS-R variables presented in Table 23 was found to be nonsignificant ($F = 1.13875$, $df = 28/74$, $P = 0.13360$). In examining the mean scores between groups it was apparent that all three groups demonstrated generally Low Average intellectual functioning, with Group 1 performing only slightly better (V.I.Q. = 89.769; P.I.Q. = 89.376; F.S.I.Q. = 88.461) than Group 2 (V.I.Q. = 84.200; P.I.Q. = 80.800; F.S.I.Q. = 81.600) and slightly better than Group 3 (V.I.Q. = 84.952; P.I.Q. = 79.238; F.S.I.Q. = 81.143). A

TABLE 23

MANOVA - 3

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING
Measures of Central Tendency
Multivariate Analysis of Variance (MANOVA)
WAIS-R Variables

	1 (N=26)		2 (N=5)		3 (N=22)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
V.I.Q.	89.77	15.13	84.20	7.26	84.95	10.40
P.I.Q.	89.38	9.97	80.80	4.87	79.24	9.39
F.S.I.Q.	88.46	11.69	81.60	3.51	81.14	8.75
Info	8.04	3.38	8.00	3.54	7.62	2.42
DS	8.15	2.41	6.80	2.28	7.48	2.38
Vocab	8.50	3.27	7.60	2.19	7.33	2.71
Arith	8.42	3.20	6.80	1.30	7.00	2.21
Comp	7.39	3.68	6.60	1.94	6.81	2.75
Sim	8.42	3.58	6.80	1.64	6.57	2.84
PC	8.62	2.89	5.40	1.67	6.86	2.44
PA	8.35	2.84	6.00	2.35	6.00	1.92
BD	9.00	2.12	8.40	3.05	7.14	2.69
OA	6.85	2.35	6.00	2.12	6.81	3.12
DSy	6.27	2.05	4.20	1.30	5.00	2.02

Manova Probability = 0.13360

Kruskal Wallis 1-Way Anova
Daily Dosage of Neuroleptic Medication by Subgroup: P = 0.1266

Mann-Whitney U - 2-Tailed P
Duration of Illness by Subgroup: P = 0.0986

minor trend evident in these scores is the Borderline mean Performance I.Q. obtained by Group 3 (Group 2 mean P.I.Q. is not much better) compared to the Low Average to Average Performance I.Q. obtained by Group 1. The 10 point discrepancy between these I.Q. values compared to the 5 point discrepancy between V.I.Q. values suggests more dysfunction to the right hemispheric functions for Groups 2 and 3.

Individual subtest scaled scores fall fairly uniformly within the Low Average range for Group 1, but both Groups 2 and 3 had many subtest scores falling within the Borderline range. The lowest subtest score for all three groups occurred on the Digit Symbol subtest. Generally, the three groups did not appear to differ substantially with respect to their intellectual functioning.

The follow-up discriminant analysis presented in Tables 24 and 25 consequently confirm this to be the case. The canonical discriminant functions revealed in Table 24 indicated a nonsignificant discrimination (Chi-Square = 35.226, df = 28, P = 0.1634) on the first function and second function (Chi-Square 12.763, df = 13, P = 0.4663).

TABLE 24

Discriminant Analysis

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING
WAIS-R Variables

	Wilks' Lambda	Univariate F	Significance
V.I.Q.	0.96	0.98	0.38
P.I.Q.	0.78	7.11	0.00
F.S.I.Q.	0.88	3.3	0.04
Info	1.00	0.12	0.89
DS	0.96	0.91	0.41
Vocab	0.96	0.93	0.40
Arith	0.93	1.90	0.16
Comp	0.99	0.25	0.78
Sim	0.92	2.13	0.13
PC	0.84	4.54	0.02
PA	0.81	5.88	0.01
BD	0.88	3.64	0.03
OA	0.87	3.81	0.03
DSy	0.87	3.65	0.03

Canonical Discriminant Functions

Function	Wilks' Lambda	Chi-Square	D.F.	Significance
1	0.4365557	35.226	28	0.1634
2	0.7485982	12.763	13	0.4663

TABLE 25

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING - WAIS-R Variables
Standardized Canonical Discriminant Function Coefficients

	Func 1	Func 2
V.I.Q.	0.82	-0.52
P.I.Q.	-1.46	3.67
F.S.I.Q.	1.35	-3.61
Info	-1.29	0.47
DS	-0.72	0.64
Vocab	0.14	0.37
Arith	-0.00	0.46
Comp	-0.70	0.37
Sim	-0.21	1.00
PC	0.53	-1.00
PA	0.84	0.13
BD	-0.39	0.36
OA	1.05	-1.04
DSy	0.78	-0.98

Classification of Results

		Predicted Group Membership		
Actual Group	N	1	2	3
1	26	20 76.9%	2 7.7%	4 15.4%
2	5	0 0.0%	5 100.0%	0 0.0%
3	21	4 19.0%	2 9.5%	15 71.4%

Percent of "Grouped" cases correctly classified: 76.92%

(c) HRNTB Performance

Again, in contrast, results from the multivariate analysis of variance conducted on the HRNTB variables, appearing in Table 26, were found to be significant ($F = 8.6452$, $df = 38/64$, $P = 0.0$). Statistically significant mean differences between these groups with respect to neuropsychological variables were found.

The univariate follow-up measure to the overall MANOVA probability statistic also revealed a number of variables that reached statistically significant levels. Specifically, all TPT measures differed significantly between Groups 1 and 2 with Group 2 being considerably more seriously impaired than Group 1. Additionally, TPTTot is statistically significantly different between all three groups with Group 1 performing the best on the task, Group 3 performing the second best and Group 2 performing the poorest.

In examining the mean levels and patterning of scores on this battery, Group 2 stood out as being a highly dysfunctional group evidencing serious levels of cerebral impairment across virtually all measures. This

group appeared to be characterized by rather diffuse and global impairment of brain functioning that is perhaps more reminiscent of Kraepelin's dementia praecox.

Group 3 also performed quite poorly on this battery, but with more variability being present in the profile patterning. The TPT performance and SSPT and SRT functions appeared most impaired, with Category and Grip Strength functions also appearing mildly impaired. This implies anterior brain dysfunction with temporal-parietal involvement along with some bilateral-frontal dysfunction.

The multivariate analysis of variance of the HRNTB variables was followed up by a discriminant analysis procedure to determine where the differences between groups occurred most prominantly from a statistical perspective. Data from this analysis are presented in Tables 27 and 28. The canonical discriminant functions revealed in Table 27 indicate that significant discrimination was achieved on the first function (Chi-Square = 130.41, df = 18, P = 0.0000) and on the second function (Chi-Square = 16.432, df = 8, P = 0.0366). Standardized canonical discriminant function coefficients listed in Table 28 under function 1 show that TPTTot, FTTDom, FTTNDom and TPTDom rank as the four variables

TABLE 26

MANOVA - 5

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING
Measures of Central Tendency
Multivariate Analysis of Variance (MANOVA)
HRNTB Variables

	1 (N=26)		2 (N=5)		3 (N=22)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Cat	63.15	31.20	102.20	19.80	73.03	27.03
TPTDom	385.39	104.41	900.00	0.0	584.70	104.64
TPTNDom	313.15	141.10	818.20	108.42	482.97	93.07
TPTBoth	844.35	186.00	2495.00	128.60	1413.10	204.70
TPTTot	844.35	186.00	2495.00	128.60	1413.10	204.70
Memory	7.23	1.45	5.00	1.40	6.09	1.30
Local	2.85	2.17	1.00	1.24	1.44	1.07
SRT	7.19	3.64	7.20	5.09	7.65	4.60
SSPT	7.00	6.54	11.40	7.30	9.41	4.92
FTTDom	46.31	7.53	31.20	12.72	40.94	6.73
FTTNDom	42.04	7.26	27.20	9.01	38.61	5.90
TrailB	96.01	50.96	102.00	51.69	169.64	96.62
GripDom	39.41	13.34	20.40	10.72	36.15	9.03
GripNDom	36.49	11.40	31.50	13.75	33.02	9.01

Manova Probability =0.0+

entered into the analysis first, thus having the greatest discriminating power. This discriminant analysis resulted in an overall 98.11% correct classification of "grouped" cases.

(d) Symptom Data

The multivariate analysis of variance of the symptom variables presented in Table 29 was found to be significant ($F = 44.2446$, $df = 11/14$, $P = 0.0$) suggesting the differences between the groups exist with respect to symptoms. An examination of the mean scores between groups indicate that Group 2 appeared to be the most symptomatic with the greatest degree of both positive and negative symptomatology; Group 3 appeared to have a reasonably high degree of positive symptoms, but fewer negative symptoms; Group 1 appeared to be the least symptomatic of the three groups.

The significant multivariate analysis of the symptom variables was follow-up by a discriminant analysis procedure to determine where the differences between groups occurred. Data from this analysis are shown in Tables 30 and 31. The canonical discriminant functions revealed in Table 30 were found to be nonsignificant on

Table 27

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING - HRNTB Variables

	Wilks' Lambda	Univariate F	Significance
Cat	0.86	3.97	0.03
TPTDom	0.28	63.92	0.0
TPTNDom	0.38	40.26	0.0
TPTBoth	0.26	71.38	0.0
TPTTot	0.13	173.9	0.0
Memory	0.84	4.748	0.01
Local	0.83	5.09	0.01
SRT	1.00	0.70	0.93
SSPT	0.97	0.89	0.42
FFTDom	0.74	8.85	0.00
FTTNDom	0.72	9.55	0.00
TrailB	0.80	6.45	0.00
GripDom	0.93	1.93	0.16
GripNDom	0.98	0.64	0.53

Canonical Discriminant Functions

Function	Wilks' Lambda	Chi-Square	D.F.	Signficance
1	0.0587227	130.41	18	0.0000
2	0.6996143	16.432	8	0.0366

TABLE 28

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING - HRNTB Variables
Standardized Canonical Discriminant Function Coefficients

	Func 1	Func 2
Cat	-0.21	-0.31
TPTDom	0.34	0.15
TPTBoth	0.17	-0.75
TPTTot	0.90	0.35
Local	-0.08	-0.49
SSPT	0.31	0.08
FTTDom	-0.86	-0.91
FTTNDom	0.45	1.44
TrailB	-0.32	0.81

Classification Results

		Predicted Group Membership		
Actual Group	N	1	2	3
1	26	26 100.0%	0 0.0%	0 0.0%
2	5	0 0.0%	5 100.0%	0 0.0%
3	22	1 4.5%	0 0.0%	21 95.5%

Percent of "Grouped" cases correctly classified: 98.11%

the first function (Chi-Square = 19.060, df = 18, P = 0.3881) and on the second function (Chi-Square = 5.3585, df = 8, P = 0.7187). Classification results of this discriminant analysis produced only a 52.83% correct classification of "grouped" cases, as shown in Table 31.

Medication levels and chronicity were again assessed as part of the analysis. The mean ranked daily dosage of neuroleptic medication (P = 0.1266) and the mean ranked duration of illness (P = 0.0986) were analysed between groups and both found to be nonsignificantly contributing factors.

(e) Summary of Cluster Analysis of HRNTB Data Subgrouping Results

In summary, three subgroupings of the schizophrenic subjects were established on the basis of a cluster analysis of HRNTB data such that Group 1 was comprised of 26 subjects, Group 2 comprised of only 5 subjects and Group 3 of 22 subjects. Descriptive analysis of mean scores for WAIS-R, HRNTB and symptom variables revealed that while the three subgroups demonstrated slight differences in intellectual functioning, significantly different neuropsychological functioning was

TABLE 29

MANOVA - 4

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING
Measures of Central Tendency
Multivariate Analysis of Variance (MANOVA)
Symptom Variables

	1 (N=26) Mean	2 (N=5) Mean	3 (N=22) Mean
Halluc	1.31	2.20	1.59
Delus	2.73	3.00	3.22
BizarreBeh	0.85	1.20	0.86
ThghtDis	1.46	2.00	2.41
AffBlunt	1.35	2.60	2.60
Alogia	1.12	1.60	0.91
Apathy	1.08	1.00	1.14
Asocial	1.12	1.60	1.68
Attent	0.42	0.40	0.73
Positive	6.35	8.40	8.09
Negative	5.08	7.20	5.32

Manova Probability = .00001*

TABLE 30

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING - Symptom Variables

	Wilks' Lambda	Univariate F	Significance
Halluc	0.97	0.87	0.43
Delus	0.99	0.24	0.79
BizarreBeh	0.99	0.33	0.72
ThghtDis	0.95	1.35	0.27
AffBlunt	0.88	3.37	0.04
Alogia	0.98	0.59	0.566
Apathy	1.00	0.38	0.96
Asocial	0.97	0.80	0.46
Attent	0.96	0.96	0.39

Canonical Discriminant Functions

Function	Wilks' Lambda	Chi-Square	D.F.	Significance
1	0.6607681	19.060	18	0.3881
2	0.8980404	5.3585	8	0.7187

TABLE 31

CLUSTER ANALYSIS OF HRNTB DATA SUBGROUPING - Symptom Variables
Standardized Canonical Discriminant Function Coefficients

	Func 1	Func 2
Halluc	0.69	0.74
Delus	-0.47	-0.37
BizarreBeh	0.68	-0.18
ThghtDis	-0.25	0.69
AffBlunt	0.80	0.26
Alogia	0.23	-0.40
Apathy	-0.31	-0.74
Asocial	-0.05	0.65
Attent	-0.50	0.17

Classification Results

Actual Group	N	Predicted Group Membership 1	2	3
1	26	11 42.3%	3 11.5%	12 46.2%
2	5	1 20.0%	4 80.0%	0 0.0%
3	22	5 22.7%	4 18.2%	13 59.1%

Percent of "Grouped Cases correctly classified: 52.83%

evident between the three groups. All three groups demonstrated Low Average intellectual functioning. Group 2 stood out most dramatically from Groups 1 and 3 as evidencing a serious degree of cerebral impairment that was characteristically diffuse and global in nature, perhaps reminiscent of Kraepelin's concept of dementia praecox. Group 2 also appeared as the most symptomatic group, characterized by a greater degree of both positive and negative symptomatology. Group 3 was characterized by scattered neuropsychological performance with bilateral, fronto-temporal functions most impaired relative to other adaptive functions, and a greater preponderance of positive compared to negative symptomatology. Finally, Group 1 stood out as the least impaired and least symptomatic group with close to Average intellectual functioning being evident, less efficient, borderline impairment of functioning of neuropsychological tests and generally fewer schizophrenic symptoms.

F. Medication Effects

Twenty-four (24) of the subjects in the study sample were unmedicated at the time of testing and 28 were medicated. Daily dosages of neuroleptic medications were computed through conversion of the various neuroleptic

medications to Chlorpromazine units.

An analysis of unmedicated compared to medicated schizophrenics was conducted. Tables 32 and 33 respectively contain the means and standard deviations for all WAIS-R and HRNTB variables for the unmedicated and medicated subjects. A nonparametric test of significance (Kruskal-Wallis 1-Way Anova) was used to determine whether or not statistically significant differences existed between the two groups on any of the variables.

(a) Research Hypotheses

In the investigation of unmedicated and medicated schizophrenic subjects with respect to their performance on the battery of tests, the following research hypotheses were formulated:

Hypothesis 1: There is no difference in unmedicated and medicated schizophrenic subjects on WAIS-R I.Q. and individual subtest variables.

Hypothesis 2: There is no difference in unmedicated and medicated schizophrenics on HRNTB variables.

(b) WAIS-R Performance

Table 32 contains the means and standard deviations for unmedicated and medicated subjects on the WAIS-R variables. For the most part, the unmedicated subjects' performance was indistinguishable from that of the medicated schizophrenics, and the null hypothesis stated at Hypothesis 1 may be accepted. Although no statistically significant differences were evident, there was a slight, nonsignificant difference in the P.I.Q. (unmedicated group mean P.I.Q. = 87.2083; medicated group mean P.I.Q. = 82.0714) that approaches statistical significance (P = 0.0748) and is worthy of noting. The unmedicated group tended to perform slightly better on the right-hemispheric visuo-spatial tasks of the Performance Scale.

(c) HRNTB Performance

Table 33 contains the means and standard deviations for unmedicated and medicated schizophrenics on the HRNTB variables. Within the brain sensitive measures of the HRNTB, again, the medicated group performed more poorly on some measures. Specifically, the Category Test was performed significantly more poorly (P = 0.0119) as

TABLE 32

Medicated and Unmedicated Schizophrenics
Measures of Central Tendency - WAIS-R Variables
Kruskal-Wallis One-Way Anova

	Unmedicated Ss (N=24)		Medicated Ss (N=28)		Level of Significance
	Mean	S.D.	Mean	S.D.	
V.I.Q.	87.42	10.38	87.18	14.83	0.52
P.I.Q.	87.21	10.14	82.07	10.36	0.08
F.S.I.Q.	86.58	9.75	83.43	11.18	0.14
Info	8.08	3.11	7.68	2.93	0.46
D.S.	7.58	2.02	7.96	2.67	0.56
Vocab	7.96	2.49	7.93	3.37	0.79
Arith	7.88	2.27	7.54	3.16	0.37
Comp	6.92	2.90	7.21	3.41	0.85
Sim	7.46	3.39	7.57	3.17	0.85
P.C.	7.21	3.01	7.93	2.62	0.27
P.A.	7.17	2.75	7.18	2.70	0.86
B.D.	8.33	2.78	8.12	2.43	0.75
O.A.	7.88	2.58	7.46	3.05	0.68
Dsy	5.79	2.21	5.36	2.00	0.52

Table 33

Medicated and Unmedicated Schizophrenics
Measures of Central Tendency - HRNTB Variables
Kruskal-Wallis One-Way Anova

	Unmedicated Ss (N=24)		Medicated Ss (N=28)		Level of Significance
	Mean	S.D.	Mean	S.D.	
Cat	82.76	30.52	60.38	26.42	0.01*
TPTDom	543.56	213.71	492.66	155.96	0.82
TPTNDom	411.24	213.37	449.20	170.52	0.19
TPTBoth	306.88	224.54	309.55	183.53	0.73
Memory	6.68	1.48	6.58	1.58	0.78
Local	2.65	1.68	1.59	1.88	0.01*
SRT	7.74	4.13	7.07	4.55	0.54
SSPT	9.68	6.69	8.10	5.25	0.39
FTTDom	43.60	10.56	41.81	7.11	0.24
FTTNDom	40.04	10.29	38.48	5.50	0.33
TrailB	126.32	74.00	143.05	93.09	0.54
GripDom	37.73	12.38	36.30	11.02	0.80
GripNDom	35.01	10.76	34.12	10.62	0.59

was the Localization score (P = 0.0146) of the TPT. In addition, the TPTNDom tended to be performed more poorly by the medicated group, although this difference is slight and is statistically nonsignificant (P = .1864). The Category Test is considered one of the most sensitive indicators of cerebral functioning. The null hypothesis stated as Hypothesis 2 above may be rejected in this instance as significant differences were evident in the unmedicated and medicated schizophrenics' performance on these tests. Combined with the significant difference evident between the two groups on the localization score, which requires incidental memory for spatial relationships or position, a trend toward poor performance on TPTNDom and P.I.Q., the medicated group appeared to be more dysfunctional for right-hemispheric functioning under the condition of neuroleptic medications.

CHAPTER VI

SUMMARY, CONCLUSIONS AND IMPLICATIONS

A. Introduction

To evaluate cognitive functioning and clinical symptom patterns, the performance of 53 schizophrenic patients on intellectual, neuropsychological and symptom rating test measures was analysed. Subjects were subgrouped into homogeneous clusters for the purpose of assessing the nature of cognitive deficit profiles and symptom patterns inherent within the subgroups. Based on the theory that these distinctly different deficit profiles may reflect distinctly different disease processes and/or pathologies, the nature of cognitive deficit patterns as they related to clinical symptom presentation was analysed.

In the review of literature presented in Chapter III, a convergence of evidence from a variety of sources led to the conclusion that brain pathology exists among many schizophrenics and that the nature of this pathology varies. Cognitive impairments have been found to be associated with structural abnormalities such as enlarged

ventricles, cerebral atrophy, reversals or absences of the normal asymmetry of the brain, changes in cerebral blood flow, and pyramidal cell abnormalities. Clinical descriptions of the schizophrenic syndrome have been characterized by a dichotomous clustering of symptoms which includes "productive" or florid symptoms, often referred to as positive symptoms and "nonproductive" or defect symptoms, often referred to as negative symptoms. These clinical symptom distinctions have been linked to specific brain deficits, and appear to reflect different patterns of brain pathology.

For example, the cerebral blood flow measures in schizophrenic populations revealed a pattern in which the whole brain was affected with either an increase in blood flow to the cerebral cortex or a decrease in blood flow to the whole brain. These whole brain increases were found to be associated with the "productive" symptoms while the whole brain decreases in cerebral blood flow were found to be associated with the "nonproductive" symptoms. In the same vein, CT Scan results have revealed some schizophrenics are characterized by whole brain atrophy and this may be analygous to these whole brain CFB anomalies.

Another pattern evident from the CBF studies is one in which only discrete areas of the brain are affected by disturbances of cerebral blood flow. Typically, these include the left anterior and left anterior and posterior. Results from CT Scan studies also reveal selected, discrete areas of brain pathology which includes findings such as reversals in the normally expected asymmetry of the brain. This brain anomally typically occurs in the absence of generalized atrophy. In effect, these findings imply different patterns of pathology among schizophrenics which reflect different disease processes.

B. Conclusions Regarding Cognitive Functioning of Total Study Population

Results of the present study of cognitive functioning among subgroups of schizophrenics similarly suggest different deficit patterns of functioning occur. Differences in mean level of performance on intellectual and neuropsychological test batteries can be used to distinguish diagnostically discrete groups of schizophrenics. Distinctly different cognitive deficit profiles and symptom patterns evident in the various subgroups of schizophrenics have often been taken as evidence in support of the notion different disease

processes or pathologies.

The cognitive functioning of the present study population of schizophrenics as a whole generally falls substantially below the normative mean values for the tests used in the study. The Low Average intellectual functioning on the WAIS-R is only slightly more spared than the adaptive functions measured by neuropsychological tests on the HRNTB, with poor cognitive functioning generally being evident within this schizophrenic group. This fact may imply deterioration of cognitive functioning that is part of schizophrenia, although premorbid comparison measures were not evaluated as part of this study. Generally speaking as well, there appeared to be an inverse relationship between symptoms and cognitive functioning in that as level of cognitive functioning deteriorated across the various subgroupings that were established within the study, the degree of symptoms present increased.

C. Conclusions Regarding Positive and Negative Symptom Schizophrenia

In the early view of schizophrenia, Kraepelin regarded this illness primarily as a defect, dementia-like

state which inevitably ran a deteriorative course. Later, however, productive features were incorporated as ancillory pathognomonic symptoms of the disorder by Bleuler, Schneider and Feighner. During the past twenty to thirty years the productive features, initially considered ancillory, have acquired prominence in diagnostic criteria for schizophrenia, while the defect state has correspondingly been minimized in importance among the diagnostic criteria.

There has been a resurgence of the delineation of the defect and productive symptoms since the start of this decade, however. Nancy Andreasen and Timothy Crow have both been instrumental in promoting a resurgence of the awareness that defect symptoms are important pathognomonic features of schizophrenia despite the fact that they have been more difficult to identify and thus historically have been less reliably measured.

Research findings of Andreasen and Crow have led them to postulate that productive and defect features of schizophrenia may represent two distinctly different syndromes, each having a different pathogenesis. The Positive symptom syndrome or Type 1 schizophrenia is hypothesized to emerge from a neurochemical disturbance in

dopamine transmission and thus is considered to be responsive to neuroleptic treatment in the resolution of positive symptoms with anticipated good prognosis; the Negative symptom syndrome is hypothesized to reflect structural brain damage, consequently resulting in poor response to neuroleptic intervention and anticipated poor outcome.

The dichotomy of positive and negative symptom schizophrenics has emerged and persisted across time as a valid construct in the research on schizophrenia. While the construct has been present for a long time, albeit under different names, research applications of the idea have been limited due to lack of reliable methods of assessing positive and negative symptoms. In this study, employing the rigorously defined diagnostic criteria for positive symptom schizophrenia and negative symptom schizophrenia established by Andreasen (1984), it is interesting to note that only 7 of 31 cases or 21% could be classified as meeting these strict diagnostic criteria for positive symptom schizophrenia and 7 of 31 cases or 21% could be classified as meeting crtieria for negative symptom schizophrenia. The largest percentage of cases were characterized by a mixture of both positive and negative symptomatology. This suggests that although the

construct remains a valid one, purely positive or purely negative symptom schizophrenics appear to form a comparatively small percentage of the total schizophrenic population, with a mixed symptom clinical picture tending to be more prevalent.

The significance of this finding that a comparatively small percentage of the study population could be classified according to Positive and Negative dimensions is the inherent implication that these constructs, although valid, are not monothetic. Results support the Positive/Negative dimension as more homogeneous subtypes of schizophrenia. However, on the basis of the results of this study, it may be stated that the delineation of schizophrenia on the basis of Positive/Negative dimensions subsumes only a small percentage of the total schizophrenic population and consequently research employing these constructs may result in a loss of valuable information as many schizophrenics are unclassifiable as having either a Positive or Negative Syndrome by virtue of having a mixed symptom pattern. In effect, research emphasis on the Positive/Negative dimensions may be somewhat misleadingly unrepresentative of schizophrenia if continued to be viewed as monothetic.

Within these rigorously defined groups of positive and negative symptom schizophrenics, distinct differences in cognitive functioning were evident, although it should be kept in mind that the number of subjects in each group was small and thus conclusions drawn should be viewed cautiously keeping this in mind. Both the level and pattern of impairment of functions for the Positive Symptom and Negative Symptom Groups differed, and these findings may be viewed as being consistent with Andreasen's and Crow's notion of different disease processes occurring for these groups.

The more purely defined Positive Symptom Group were defined by relatively normal intellectual functioning, showing fewer intellectual deficits than the Negative Symptom Group, tending to function somewhat more normally, although at the lower end of the Average Range intellectually. The pattern of cognitive functioning for the Positive Symptom Group could be described as a less disturbed pattern of cerebral dysfunction, perhaps analogous to Crow's Type 1 description of schizophrenia (Johnstone, Crow, Frith, 1978). Andreasen (1982) suggests that for this type of schizophrenic there is a "release from higher cortical inhibitors" which produces a reduction of efficiency of cerebral functions. Within this

model, functional deficits are said to occur as a result of a loss of inhibitory functions which are, in effect, characterized by a primary loss of control of information processing such as the ability to organize information meaningfully and purposefully. This loss of information processing due to the loss of cortical inhibitory functions conceivably could fit the dopamine hypothesis of schizophrenia in which neural synapses are overactive with dopamine and thus result in less efficient information processing. Generally, far less cerebral compromise was present for this Positive Symptom Group. This group appeared to be characterized by a degree of impairment from which rather mild dysfunction, perhaps of a neurochemical nature, could be inferred, and it may be reasonable to conclude that the Positive Symptom Syndrome of schizophrenia may be more therapeutically amenable to neurochemical intervention, as is already indicated by the research literature on this topic.

The more purely defined Negative Symptom Group, in contrast, was characterized by a greater degree of impaired cognitive functioning. More scattering of subtest scores on the WAIS-R was evident with Vocabulary, Comprehension and Similarities subtests on the Verbal Scale being most poorly performed, implying a deficit for

left-hemispheric language functioning. Bilateral gross motor grip strength (implicating bilateral frontal lobes), Category Test performance (implicating left and/or right prefrontal regions) reflecting general thinking ability and logical analysis, SRT performance (temporal lobe) requiring complex attention and concentration as well as auditory discrimination of patterns of rhythms also tended to be more impaired in this group compared to the Positive Symptom Group. In effect, this group was characterized by a pattern of bilateral frontal-temporal impairment, with emphasis of impairment being evident in left-hemispheric language functions.

The observed relationship between negative symptoms such as alogia, avolition and apathy is precisely what one would predict to be related to frontal system abnormality and this is born out in the present deficit pattern results for the Negative Symptom Group. It has been hypothesized that such abnormalities may reflect some type of early disturbance (e.g., subclinical viral infections) that has led to early developmental abnormalities such as reversals in or lack of normal brain asymmetries and thus affected functional "specialities" of these areas of the brain.

In effect, the deficit pattern of the Negative Symptom Group appeared to evidence a degree and pattern of impairment from which structural brain damage may be inferred. It is reasonable to presume that although a certain amount of elasticity is present in the human brain, structural damage is clearly less resiliant and amenable to intervention and thus undoubtedly contributes to the poorer prognosis that is typically associated with the presence of negative symptoms.

The negative symptom pattern has become connected with Kraepelin's original concept of a dementia praecox and negative symptoms have generally become equated with a bleak deteriorating outcome. The present results coincide with this notion in that results reflected the fact that the Negative Symptom Group performed more poorly when compared to the Positive Symptom Group and this fact did not appear to be a function of duration of illness, as no differences between the two groups were evident in this respect. However, it is interesting to note that this more purely defined Negative Symptom group was NOT the most malignant group in the present study.

D. Conclusions Regarding Mixed Symptom Schizophrenia

The largest percentage of schizophrenics in this study were characterized by mixtures of both Positive and Negative symptoms. Further subgrouping of the subjects beyond the positive/negative dichotomy revealed a particularly malignant subgroup of schizophrenics who were defined by serious compromise of cognitive functions and who were simultaneously highly symptomatic. This small subgroup, forming 9.04% of the total sample, were characterized by severe cognitive impairment which was characteristically global and diffuse in nature, although a greater left-hemispheric emphasis was still discernible. Virtually all cognitive functions assessed for this group reflected a serious degree of impairment. In addition, this group was distinctly more seriously symptomatic with a preponderance of both positive and negative symptomatology of virtually equal magnitudes.

More than others studied as part of this project, this highly impaired and symptomatic group appeared to most closely resemble the Kraepelinean concept of a dementia in which extreme impairment of cognitive functions was evident. This pattern of global, diffuse impairment perhaps also is one within which one might infer an atrophying process which globally affects functional abilities. Alternatively, it may represent more

than one pathological process occurring simultaneously. It is noteworthy to observe that BOTH positive and negative symptoms were present in this seriously pathological group. As a specific observation in this regard, it appears as though dementia-like schizophrenia is not necessarily exclusively related to a negative symptom syndrome as Crow and Andreasen have suggested. Clearly, from the present findings serious degrees of both Positive and Negative symptoms may be present and be associated with a serious degree of global cognitive impairment resembling a pattern of neuropsychological impairment that one might expect from structural brain damage. It may be argued from this observation of the presence of both Positive and Negative Symptoms, as has been suggested by Liddle (1987) that if symptoms from two apparently different syndromes (e.g., Positive and Negative Syndromes) can occur in the same schizophrenic individual, then the syndromes "do not represent different types of schizophrenia, but instead reflect discrete pathological processes occurring within a single disease".

This particularly malignant subgroup of schizophrenics undoubtedly is similar to those described in the literature as having cerebral atrophy and/or whole brain changes in cerebral blood flow. Accentuation of

impaired left-hemispheric functions was present within this group within the context of more generalized impairment of cognitive functions and increased prevalence and severity of symptoms. The severity of left-hemispheric impairment may have resulted in a disturbance to right-hemispheric functioning as well in that the right-hemisphere becomes unable to preferentially select information for which it is specialized (e.g., visual-spatial information) because the left hemisphere is not performing its inhibitory function. Left-brain functioning necessarily is inhibited under normal circumstances of brain processing in order to allow the right-hemisphere to perform specialized functions. The left-hemisphere, due to the deductive, step-wise, sequential specialization becomes overloaded when it is unable to inhibit processing of this type of information, and logically would produce a global, diffuse pattern of cognitive and language deficits and thus lead to ideosyncratic interpretations of the world which would be seen as schizophrenic symptoms. The simultaneous presence of both positive and negative symptoms within the context of such severe cognitive impairment may be explained in this way, where disturbed activation of brain functioning in both hemispheres results in more severe functional impairments. The disturbed activation of both hemispheres

may reflect the presence of more than one pathological process occurring simultaneously, contributing to a more serious clinical presentation.

A relationship between the degree of symptoms present and the degree of cognitive impairment appeared evident in this study in that typically a greater preponderance of symptoms were present under the coexisting presence of increasing levels of cognitive impairment. This reinforces the notion that brain pathology exists among schizophrenics that bears a distinct relationship to the schizophrenic symptoms.

Another pattern evident in the analysis of these schizophrenic subgroups was an apparent deterioration of right hemispheric functions. When subgroups with increasing levels of cognitive impairment were compared to relatively intact subgroups, it was evident that the right-hemispheric functions distinguished these groups, with greater compromise occurring in these right-hemispheric functions as part of the notable qualitative differences between the groups. A conclusion that may be drawn from this is that while schizophrenia may initially be characterized by an emphasis in left-hemispheric dysfunction, as the illness progresses,

if the symptoms are not resolved, secondary deterioration of right-hemispheric functions may occur producing a more global pattern of impairment.

It has often been argued that duration of illness is a factor that significantly relates to the clinical presentation of the illness. This is undeniably true; however, it may also be stated that different presentations of schizophrenia are not simply a manifestation of different phases of the same illness relating to duration. The fact that there were no significant differences in duration of illness between the Positive and Negative Symptom subgroups, nor between the Impairment Index Subgroups, nor between the Cluster Analysis of HRNTB data Subgroups may be argued as evidence in support of the notion that the symptom states are not sequentially occurring aspects of the illness but are instead discrete pathological processes that may be present for any given schizophrenic individual.

B. Conclusions Regarding the Effects of Neuroleptic Medications

Based on the findings in this study, it appears possible that neuroleptic medications may actually

interfere with right hemispheric functions, although presumably effectively facilitating left-hemispheric functions. In comparing unmedicated and medicated subjects, medicated subjects performed significantly more poorly on a number of tests. It may be concluded from this that the medications actually interfered with some cognitive functions. The right-hemispheric functions appeared to be most implicated. If it is also true that secondary right-hemispheric compromise occurs in some schizophrenic subtypes as a progressive function of the illness, it may be inferred also that there are clinical implications of the utilization of neuroleptic medications that require consideration. In this case, assessment of both symptom and cognitive deficit patterns are likely to be useful in the treatment of schizophrenia. Both of these hypotheses, however, require further investigation.

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APPENDIX A

Scale for the Assessment of Positive Symptoms

SCALE FOR THE ASSESSMENT OF POSITIVE SYMPTOMS

(SAPS)

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